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ANGIOTENSIN, ALDOSTERONE AND HUMAN ARTERIAL HYPERTENSION*

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THIS ARTICLE outlines the history of the continuous pursuit of a research problem throughout a 12-year period and will be presented in chronological order from the time this work was started at the Rockefeller Institute in 1948. It deals with the work carried out at the Clinical Research Department of the Hôtel-Dieu Hospital, Montreal, on the mechanism of human arterial hypertension, especially from the point of view of the relationships of sodium, the adrenal cortex and the kidney in the pathogenesis of this disease. The working hypothesis for this project was based on the following clinical and experimental evidence.

Relation Between Sodium and Arterial Hypertension[1]

A high-sodium intake potentiates the hypertensive effect of most corticosteroids. On the other hand, diets in which sodium is restricted to below 250 mg. per day, natriuretic drugs of the thiazide series or chlorthalidone and aldosterone antagonists or inhibitors exert a hypotensive effect, especially in the early benign phase of the disease. It has been found that excessive salt intake for prolonged periods can produce arterial hypertension in rats and chickens and in humans. Dahl[2] has given some indirect evidence of the correlation between the incidence of hypertensive cardiovascular disease and the excessive sodium intake of certain populations. Friedman[3-5] has demonstrated both in adrenalectomized rats and dogs a relationship between an increase in blood pressure and the rate of sodium transfer towards the intracellular compartment. Tobian[6-9] has found significantly higher ($p < 0.001$) than normal amounts of intracellular sodium in the arterial walls and striated muscles of hypertensive dogs and humans. After a salt load, the amount of sodium excreted represents up to 10-12% of the sodium filtered in hypertensive subjects or animals in contrast to 3-4% in normal subjects. As Cottier *et al.*[10] have recently shown, this is especially so in the less severe stage of hypertensive disease before any severe impairment in the renal plasma flow and glomerular filtration rate occurs.

Relation Between the Adrenal Cortex and Arterial Hypertension

A relationship between the adrenal cortex and arterial hypertension is also quite clear, both from the clinical point of view and from experimental evidence. From the clinical aspect, adrenal insufficiency (or Addison's disease) is always accompanied by a very low blood pressure. On the other hand, hypertension is found in all reported patients with primary aldosteronism, in 85% of patients with Cushing's syndrome, in the hypertensive form of congenital adrenal hyperplasia with its excessive formation of desoxycorticosterone and its 17-hydroxy derivative, and in many patients with adrenocortical carcinomas. Most corticosteroids, especially desoxycorticosterone, the 9α-fluoro- or chloro- derivatives of cortisol, 17-hydroxy, 11-desoxycorticosterone (Compound "S") and aldosterone, show hypertensive effects which are especially marked when the diet contains a normal or high amount of sodium.

Experimentally, hormonal hypertension is easily produced by administration of a high-salt diet or of desoxycorticosterone or most corticosteroids. Although Fregly[11] was able recently to induce hypertension in adrenalectomized rats with encapsulated kidneys, maintained on 0.9 g. % sodium chloride solution as drinking fluid, the presence of some portion of the adrenal cortex and of a certain amount of sodium in the diet is necessary for the development or the maintenance of almost all forms of experimental hypertension. In uni-nephrectomized and uni-adrenalectomized rats, regeneration of the remaining adrenal, previously incised and emptied of its content, is often followed by severe hypertension. The work of Deane and Masson,[12] Tobian[1, 6-9, 13] and Hartroft *et al.*[14-18] has established a very close correlation between the width of the zona glomerulosa, the granulations of the juxta-glomerular cells and the renal renin content in response to changes in dietary sodium and blood pressure. It has also been established that the width of the zona glomerulosa increases in rats with experimental renal hypertension or after renin administration.[12] In addition, the weight of both adrenals from patients who have died from severe or malignant hypertension is often found at autopsy to be several grams greater than that of normotensive patients who have died from other causes.

Previous Work

When our investigations were begun in 1948 at the Rockefeller Institute on the measurement of urinary corticosteroids in hypertensive patients, most of the foregoing evidence was known, but the

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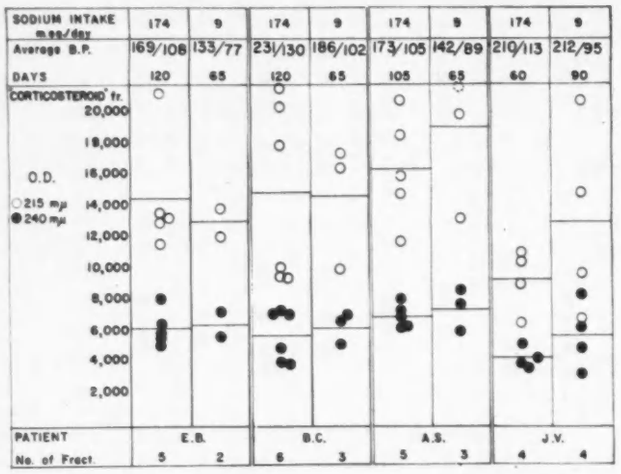

Fig. 1.—Crude lipid extracts of urine were fractionated on aluminum oxide columns. The corticosteroid-containing fraction, when measured by its ultraviolet absorption at 240 mμ. (black dots), does not show any difference during periods of high sodium intake (174 mEq./day) and high blood pressures, compared with periods of severe sodium restriction (9 mEq./day) and marked decrease in diastolic blood pressures. Each dot represents the measurement performed on one urine during the periods of observation of high and restricted salt intake. The horizontal line of each column is the mean value for the number of urines studied during each period.[19]

methods for separating and measuring adrenocortical steroids were very crude. Using an aluminum oxide column for fractionation of lipid extracts of urine, a corticosteroid-containing fraction eluted by water was isolated. As shown in Fig. 1, no difference could be established by the ultraviolet measurement at 240 millimicrons (mμ.) of the corticosteroid fraction between the values obtained in the same hypertensive patients during periods of a 4-g. sodium intake and high blood pressure levels and those obtained during periods of severe sodium restriction and marked lowering of blood pressure to normotensive levels in almost all patients.[19] The method was not sufficiently sensitive to detect changes smaller than about 100 micrograms (μg.) per day and was non-specific in comparison with the newer techniques available.

A. *Aldosterone*

After the discovery of aldosterone in adrenal extracts by Simpson and Tait[20, 21] in 1952, we restudied the problem at the Hôtel-Dieu Hospital, using the newer procedures of paper chromatography and biological assay for sodium-retaining activity, as suggested by Simpson and Tait. After extraction of urine following pH 1 hydrolysis for 24 hours, and again after β-glucuronidase hydrolysis, and subsequent fractionation of the extract, first on Zaffaroni's propylene glycol/toluene system[22] and then on the Bush C system of toluene ethyl acetate/aqueous methanol,[23] the purified aldosterone fraction obtained after the second paper chromatographic separation was determined by a rat assay method modified from that of Singer and Venning.[24] When a fraction of the purified extract, equivalent to a 40-minute urine output, was injected into adrenalectomized rats, the decrease in urinary Na/K ratio, which was used as

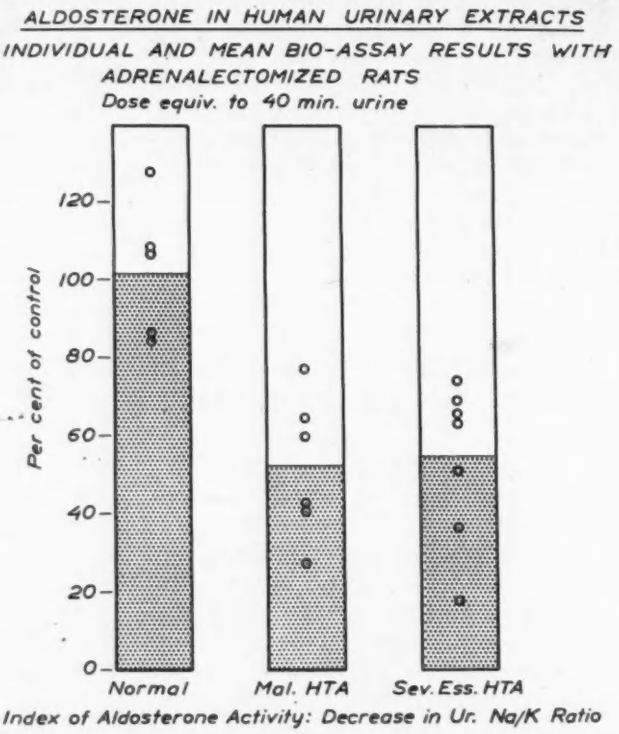

Fig. 2.—The decrease in urinary Na/K ratio of adrenalectomized rats is used as the index of activity of the purified aldosterone fraction. The individual results (circles) from five normal subjects, six patients with malignant hypertension and seven with severe essential hypertension are indicated. The differences of the means (horizontal lines) of the two groups of hypertensive patients compared with that of the normal control group are highly significant ("p" < 0.001). This figure is a modification of that published in *Science*, 123: 503, 1956, and reproduced with their kind permission.

the index of aldosterone activity, was highly significant ($p < 0.001$) in the group of rats receiving the extract of urine of hypertensive patients in comparison with those receiving extracts of urine from normotensive subjects (Fig. 2). This finding suggested for the first time, in 1956, that hyper-

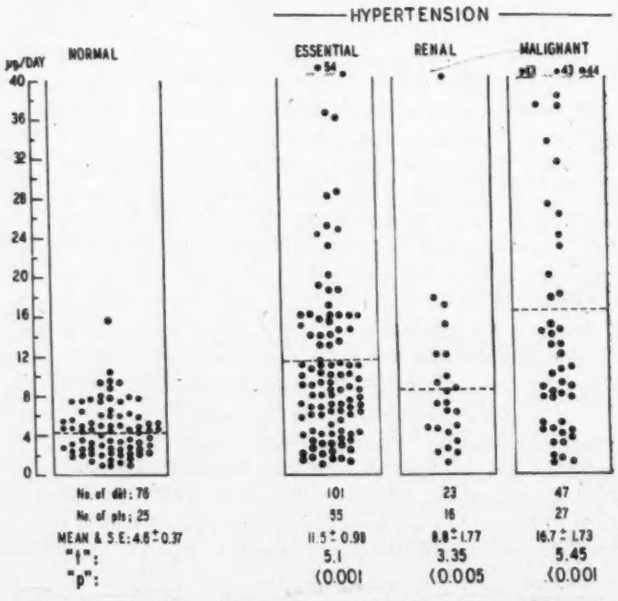

Fig. 3.—Results of urinary aldosterone obtained by the specific procedure of Nowaczynski, Koiw and Genest.[21] The "t" and "p" values indicate the high significance of the differences in the mean aldosterone excretion between the three groups of hypertensive patients compared with that of normal subjects.

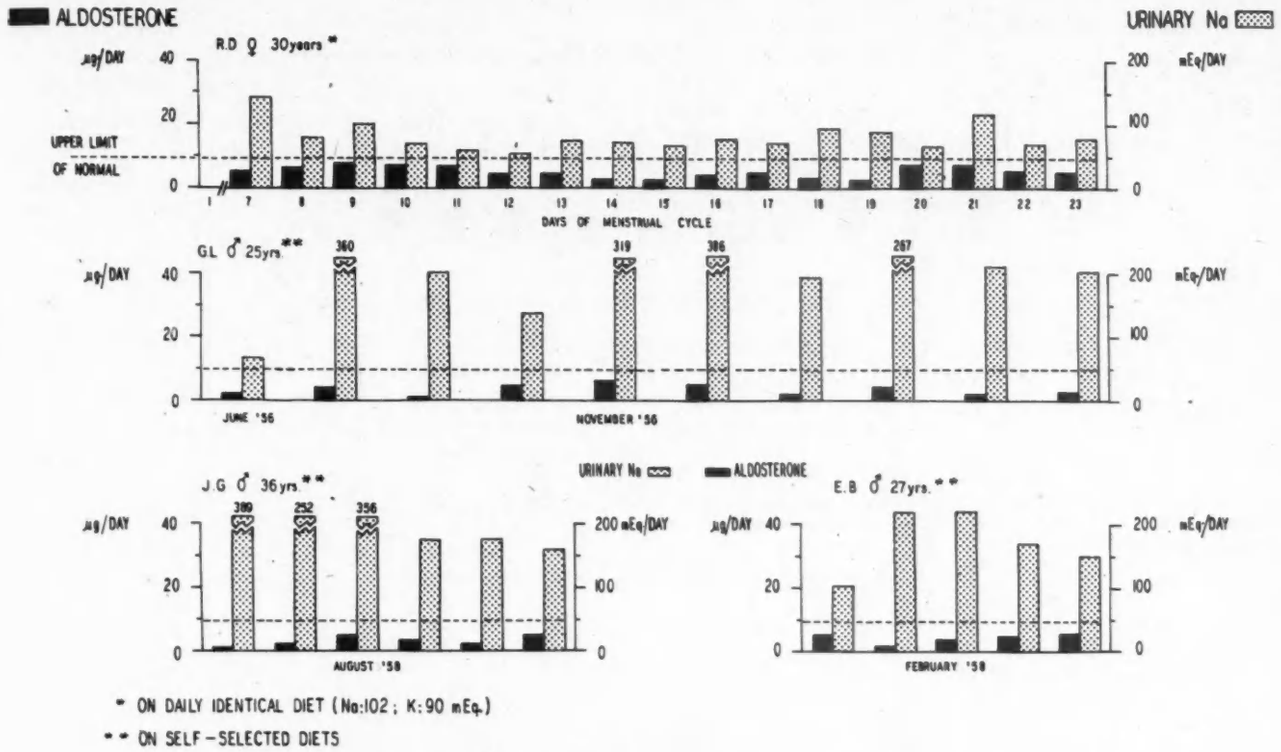

Fig. 4.—The daily urinary aldosterone and sodium excretion in these four normal subjects remains well within normal limits, despite great variation in the sodium intake and the fact that these normal subjects were carrying on their usual activities. Subject R.D. (upper part) was maintained through a whole menstrual cycle on a daily identical diet (Na: 102; K: 90 mEq./day) of exactly the same foods in the same amounts and the same volume of fluid intake from day to day.

tensive patients excreted, on the average, more aldosterone than normotensive subjects.[25]

However, we soon became dissatisfied with the biological assay for sodium-retaining substances in adrenalectomized rats, since it lacked specificity and accuracy, especially if the urinary extracts were not sufficiently purified and if only one time-dosage equivalent was used. In addition, this bioassay was very costly of labour, animals and material; it allowed considerable variations and was often quantitatively inaccurate. Furthermore, results obtained with this type of bioassay in several laboratories were often contradictory.

It was also found, by Nowaczynski in our laboratory, that the purified aldosterone fraction isolated was a mixture which contained possibly seven other substances interfering in various degrees with the accurate determination of aldosterone.[26] This led to a more extensive fractionation of the neutral urine extract by the use of three different paper chromatographic systems and the isolation of aldosterone in a very high degree of purity.[27]

In 1958, we reported our findings concerning urinary aldosterone in patients with various types of arterial hypertension as estimated by our new physico-chemical method of aldosterone determination.[28] It was possible to demonstrate, in a reasonable number of normal subjects and hypertensive patients, a twofold increase in mean urinary aldosterone excretion in patients with essential, renal and malignant hypertension as compared with that of normal subjects. This difference was highly significant, with a "p" value below 0.001. In addition, urinary aldosterone was found to vary excessively from day to day in the urine of hypertensive patients, in contrast to the quite stable excretion of urinary aldosterone in normal subjects. No reasons, such as acute stress, anxiety state, or the level of sodium or potassium intake, could be found to account for these variations, and no correlation could be demonstrated between the sodium intake or the urinary Na/K ratio and urinary aldosterone in normal subjects or hypertensive patients.

In November 1960, we reported the results of an extensive study of a large steroid spectrum in the urine of normal subjects and hypertensive patients.[29] The classification of hypertensive disease and the various chemical or physicochemical methods used for fractionation, purification and determination of steroids have been previously reported.[29-34] The determination of each of the steroids analyzed was made after extensive purification. None of the hypertensive patients studied presented any edema or signs of congestive heart failure. The normal subjects and hypertensive patients were on unrestricted diets, save for about half of the patients with malignant hypertension who were not permitted the use of added salt.

Two hundred and forty-seven determinations of urinary aldosterone were made by our procedure in 123 normal subjects and hypertensive patients. The results showed a twofold to fourfold increase in mean urinary aldosterone excretion in patients with essential, renal and malignant hypertension

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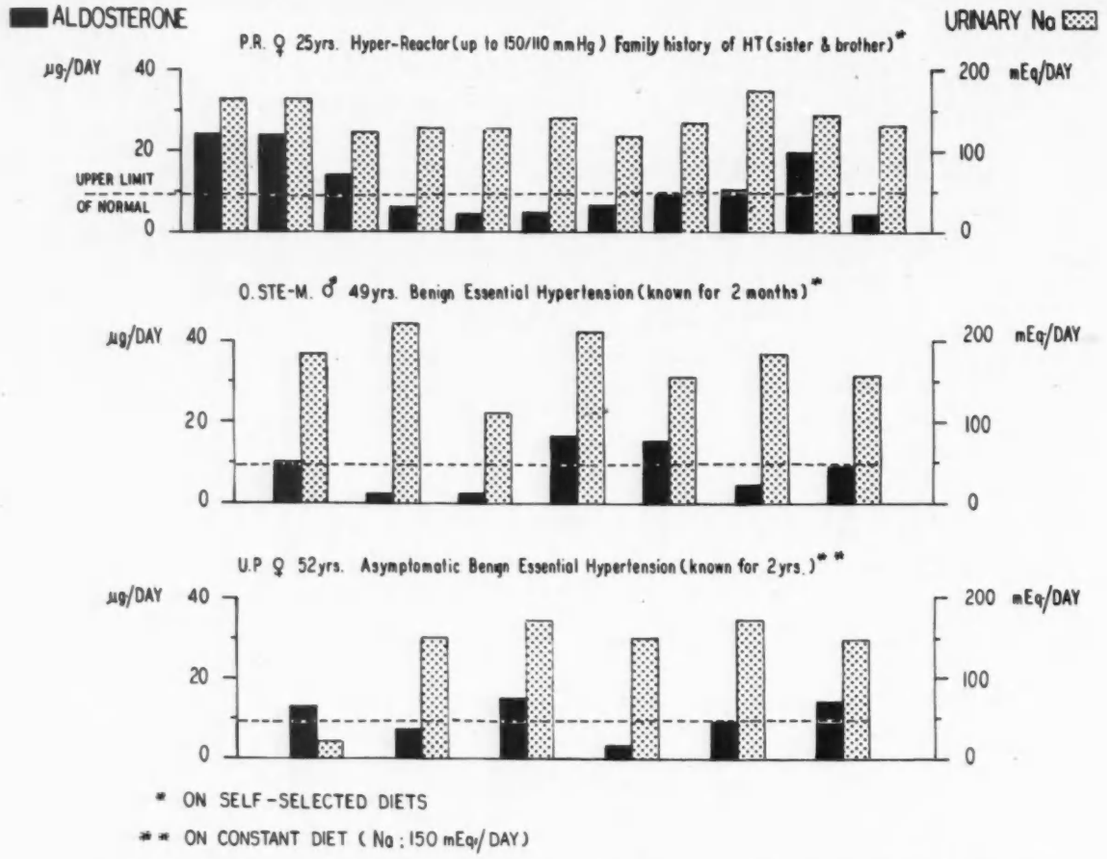

Fig. 5.—These three patients with benign essential hypertension show excessive fluctuations in urinary aldosterone in contrast to the quite stable excretion in normal subjects.

compared with that for normal subjects similarly studied (Fig. 3). Differences between means are statistically significant for the groups of essential ($p < 0.001$), renal ($p = 0.005$) and malignant ($p < 0.001$) hypertension. Forty-three per cent of all aldosterone determinations in patients with essential and malignant hypertension were above the upper limits of normal (2 to 10 μg. per day).

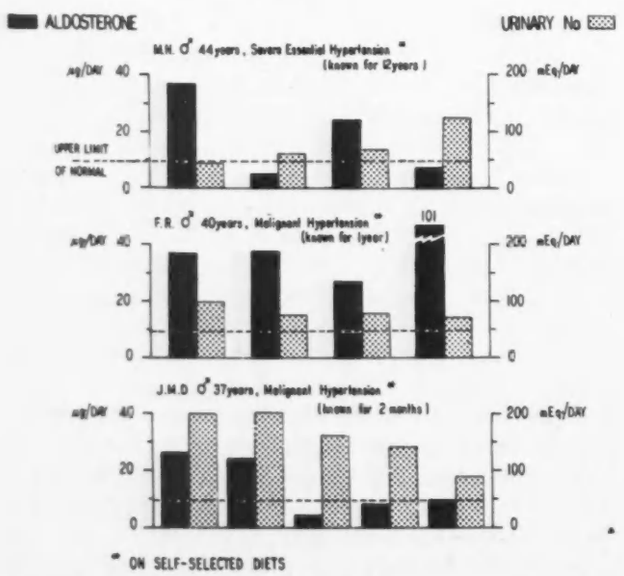

Fig. 6.—In patients with severe and malignant hypertension, the fluctuations in daily urinary aldosterone excretion are even more marked than in those with the more benign form of the disease.

These results are derived from spot determinations on hypertensive patients. It is obvious that marked overlapping exists in individual values obtained in normal subjects and hypertensive patients. For this reason, several normal subjects and patients with various types of hypertension were followed up with daily determination of their aldosterone for periods of five to 20 consecutive days. Some of these were on self-selected diets and others on a fixed sodium and potassium intake. As shown in Fig. 4, daily urinary aldosterone excretion of normal subjects, whether on a self-selected or on a fixed diet containing 102 mEq. of sodium and 90 mEq. of potassium per day, remained well within normal limits, even when these subjects were carrying on their usual activities, and despite marked variations in daily sodium intake in some subjects. On the other hand, all of the hypertensive patients but one showed, under conditions of hospitalization, excessive fluctuations in daily aldosterone excretion from normal to above normal levels (Figs. 5 and 6). Such fluctuations are more marked in the severe and malignant forms of hypertensive disease but are also present in patients in the asymptomatic phase of benign essential hypertension and were found in one patient with coarctation of the aorta and another with pheochromocytoma. These occasionally high levels of urinary aldosterone excretion cannot be explained on the basis of edema (which was absent) or on

the basis of stress, anxiety state, sodium restriction or excessive potassium intake.

The finding of a mean increase in urinary aldosterone in hypertensive patients has been repeatedly confirmed, especially by Venning *et al.*,[35] Tronchetti *et al.*,[36, 37] Romanelli *et al.*,[38, 39] Dispensa,[40] Gornall *et al.*,[41] Gherasimov,[42] Warter *et al.*[43, 44] and Garst *et al.*[45] All of these workers, using either our procedure or that of Neher and Wettstein[46, 47] or some modifications thereof, have obtained almost identical findings. Venning[35] and Romanelli,[39] especially, have extended our observations of excessive daily fluctuations in urinary aldosterone in patients with primary benign hypertension. On the other hand, Laragh and coworkers,[48] while confirming the excessive aldosterone secretion rates of patients with severe or malignant hypertension, reported normal secretion rates in less severe cases. Although the findings of Laragh *et al.* in malignant hypertension have not been confirmed in preliminary studies by Muller[49] or by Beck[60] in two such patients, the discrepancies found between the normal aldosterone secretion rate and the excessive fluctuations of urinary aldosterone in patients with primary benign hypertension may indicate a difference between hypertensive patients and normal subjects in their metabolism and/or their excretion of the hormone.

B. *Pregnane-3α, 17α, 20α-triol*

We found a highly significant decrease ($p<0.001$) in mean pregnanetriol excretion in groups of patients with essential, renal and malignant hypertension as compared with that of normal subjects.

TABLE I.—URINARY PREGNANETRIOL

		Hypertension		
	Normal	*Essential*	*Renal*	*Malignant*
(A) Bongiovanni and Eberlein's Procedure				
No. of determinations	11	33	9	15
No. of patients	10	26	8	12
Mean and S.E.	2105±271	991±119	698±150	770±159
"t"		4.14	4.06	4.3
"p"		<0.001	<0.001	<0.001
(B) Nowaczynski-Koiw-Genest's Procedure				
No. of determinations and patients	20	32	5	18
Mean	945	362	161	254
"t"		4.97	3.44	5.03
"p"		<0.001	<0.005	<0.001

The similar results obtained by Bongiovanni and Eberlein's method[51] and by the more specific procedure of Nowaczynski, Koiw and Genest[32] are shown in Table I. With the procedure of Nowaczynski *et al.*[32] there is a much lesser degree of overlapping and a greater number of pregnanetriol values below the lower limits of normal in hypertensive patients.

C. *Urinary Pregnanetriol/Aldosterone Ratio*

Since the excretions of these two substances in hypertensive patients vary in opposite directions, their ratio may become a more sensitive index of hypertensive cardiovascular disease. Results obtained by the simultaneous determinations of urinary aldosterone and pregnanetriol (by Bongiovanni and Eberlein's method or by the procedure of Nowaczynski, Koiw and Genest) in the same patients are shown in Table II. This ratio in all of the three groups of hypertensive patients (essential, renal and malignant) is below the lower limits of the normal range in 92% of all patients studied by these two methods.

TABLE II.—URINARY PREGNANETRIOL/ALDOSTERONE RATIO

		Hypertension		
	Normal	*Essential*	*Renal*	*Malignant*
(A) Bongiovanni and Eberlein's Procedure				
No. of determinations	11	31	8	12
Mean:	*358*	*104*	*104*	*51*
	(92% below normal limits)			
(B) Nowaczynski-Koiw-Genest's Procedure				
No. of determinations	8	32	4	17
Mean	*134*	*29.7*	*15*	*24*
	(92% below normal limits)			

Whether there is an absolute increase in aldosterone or a relative excess over a decreased pregnanetriol (which is derived mainly from progesterone after 17-hydroxylation), this ratio appears to be quite an important index of the hypertensive process. Of possible significance in this regard are the studies of Landau,[52] Kagawa[53] and Gornall[54] which showed that progesterone inhibits the sodium-retaining effect of aldosterone and for this reason has been called an aldosterone antagonist.

The value of these studies is illustrated by the following case (Fig. 7). In January 1959, urinary aldosterone from a 23-year-old girl, used as normal control, and believed to be normotensive on the basis of a single blood pressure reading, was found to be excessively high and the pregnanetriol/aldosterone ratio much below the lower limit of normal range. When these results became known in March 1959, blood pressure readings were taken twice a day for two weeks and showed on several occasions systolic readings of 140 and 142 mm. Hg and diastolic readings of 90 and 92 mm. Hg. Serial daily aldosterone determinations showed marked fluctuations from normal to abnormally high levels, such as are encountered in benign hypertension, and the pregnanetriol/aldosterone ratio was again much lower than normal. At this point it was ascertained that a brother and a sister of this patient were suffering from hypertension. In September 1959, her blood pressure, taken twice daily for a week, was found to be occasionally elevated to 140/110 and 150/100 mm. Hg. It is significant that this young girl, believed to be normotensive, was found, through urinary determinations of aldosterone and pregnanetriol, to have fluctuations in

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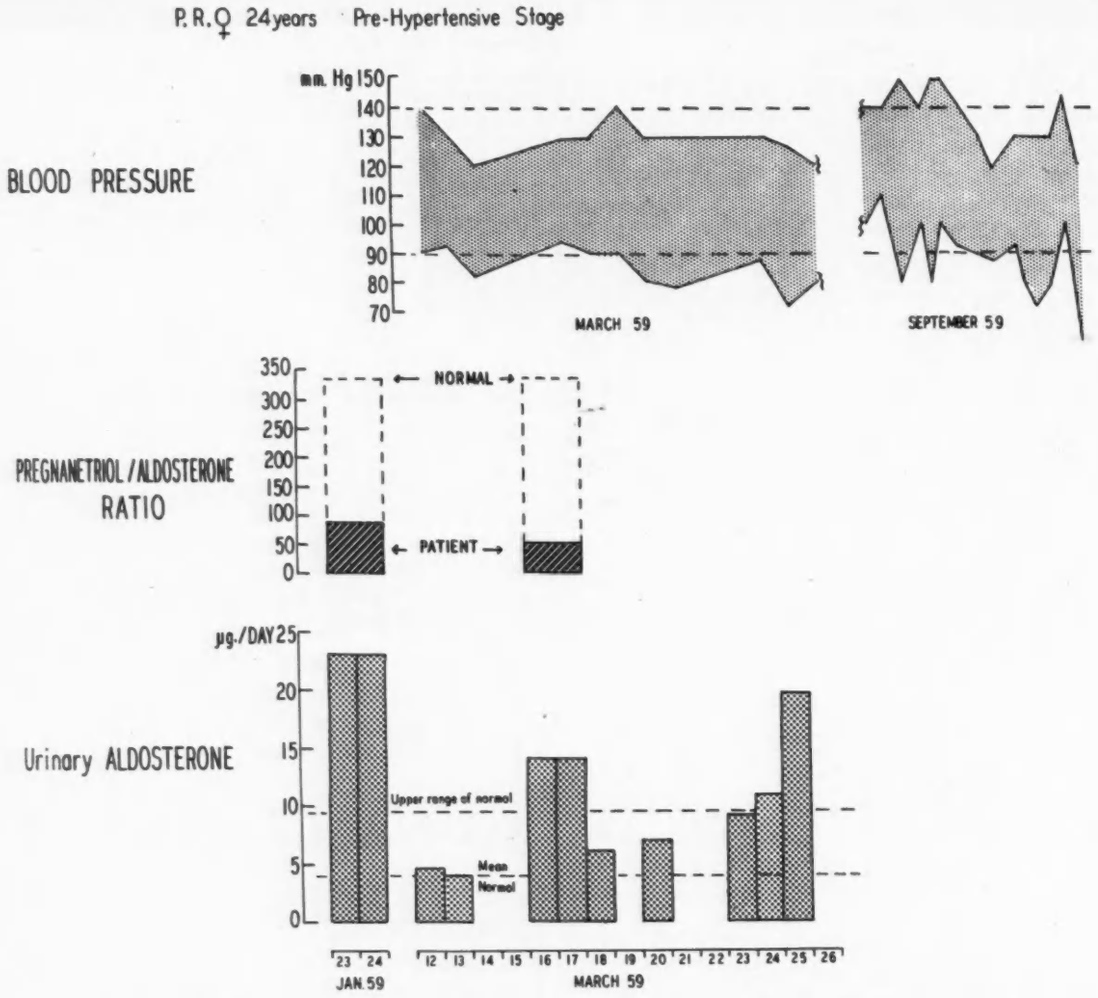

Fig. 7.—See text. (This figure is reproduced through the courtesy of *Acta endocrinologica*.[29])

blood pressure up to hypertensive levels and to have a family history of hypertension.

D. *Other Corticosteroids*

There is no significant difference in the mean excretion of the other steroids, cortisol, cortisone and their tetrahydro derivatives, etiocholanolone and the tetrahydro derivative of 17-hydroxy,11-desoxycorticosterone, in groups of patients with essential, renal and malignant hypertension as compared to that of normal subjects.

E. *Effects of Angiotensin Infusions**

Although the foregoing findings appear to be of significance, it is difficult, and indeed impossible, to overlook the role of the kidney in view of the clinical and experimental evidence linking this organ to hypertensive cardiovascular disease. In addition, there is strong experimental evidence showing a close correlation between the renal juxtaglomerular cells, the adrenal zona glomerulosa and sodium regulation, as outlined in Tobian's recent comprehensive review.[1] It was therefore logical to undertake a study of the relationships between aldosterone, sodium regulation, and the renal pressor mechanism, specifically angiotensin, which had just been synthesized by Schwyzer *et al.*[55]

The angiotensin used in these experiments was the synthetic preparation, valine-5 angiotensin II, aspartic β-amide.† This angiotensin is identical to that isolated from oxen, by Elliott and Peart,[56] except that the aspartic acid is replaced by asparagine in the synthetic material.

Acute and long-term intravenous infusions of angiotensin dissolved in 5% glucose were administered to normal subjects and benign hypertensive patients. Studies were made on urine volume; sodium and potassium excretion; glomerular filtration rate, as approximately measured by creatinine clearance; and urinary aldosterone, cortisol, cortisone and their tetrahydro derivatives. The technical procedures used in these experiments have already been described.[29, 31, 57]

Twelve volunteer medical students and two normotensive women with anxiety neurosis were used as normal controls. Six hypertensive patients in the early benign phase of essential hypertension were studied. All subjects were maintained on a

*I would like to thank Dr. Pierre Biron for his collaboration in these investigations.

†Ciba Company, Preparation 19990-A.

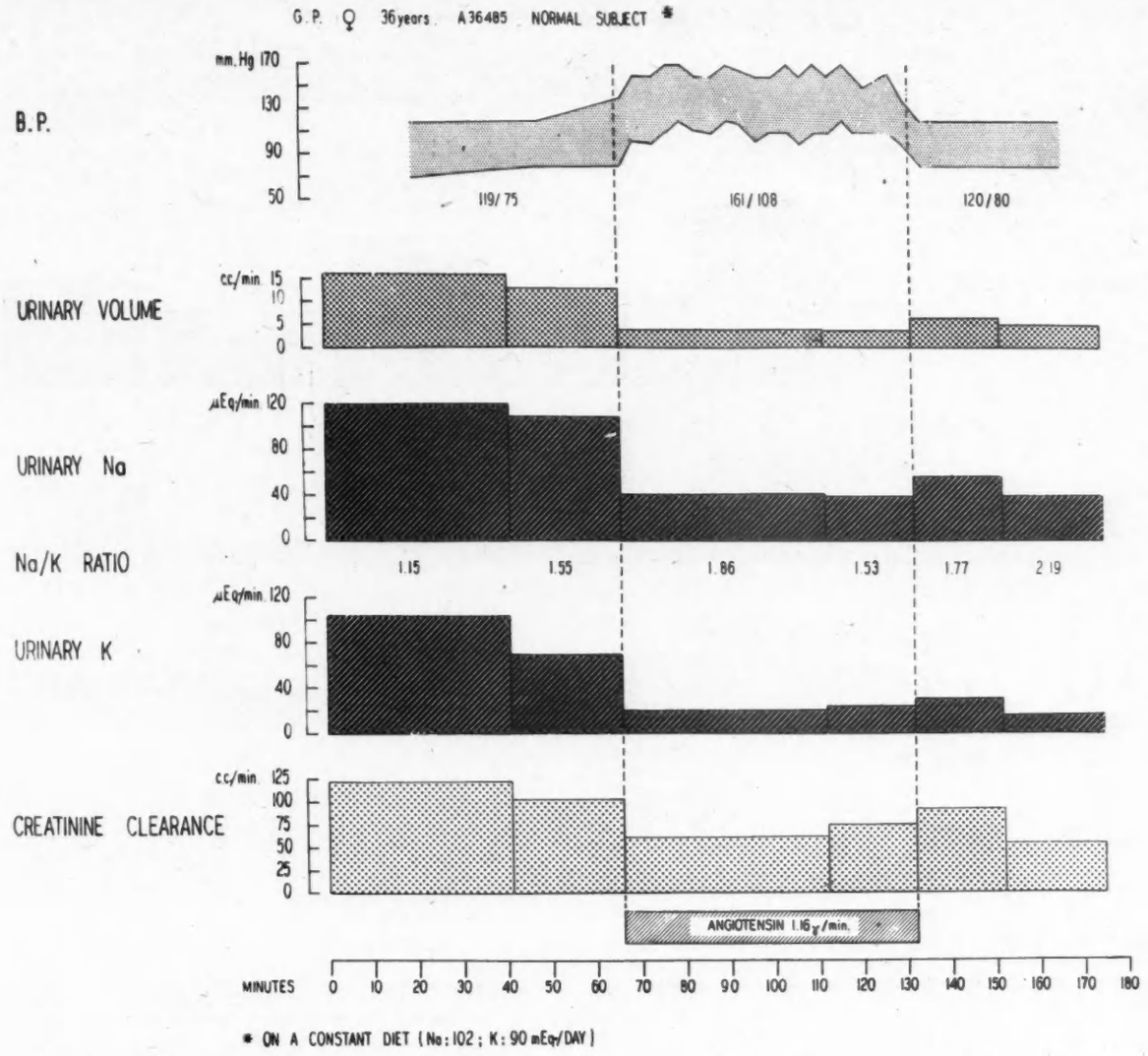

Fig. 8.—Effect of angiotensin infusion (1.16 μg./min. for 70 min.), given at a rate productive of a hypertensive level to a normal subject (G.P.), on urinary volume, sodium, Na/K ratio, potassium and creatinine clearance used as an approximate measurement of the glomerular filtration rate. There is a marked fall in creatinine clearance accompanied by a significant degree of sodium and potassium retention.

fixed sodium and potassium intake (102 and 90 mEq. per day, respectively) for periods of five to six days prior to and during the whole experimental period, under metabolic balance conditions. Urines were collected daily. When infusions were given, urines were collected during the period of infusion and again separately for the rest of the 24-hour period. All results of urinary aldosterone and steroid determination are expressed on a daily basis.

(1) *Effects of Angiotensin on Urinary Electrolytes and Creatinine Clearance*

These experiments were designed to study the effects of angiotensin infusions administered at rates productive of hypertension (increase of 18 to 30 mm. Hg in diastolic pressure above control levels) for 40 minutes to 8 hours in six normal subjects and two patients with benign essential hypertension. All results of creatinine clearances are corrected to 1.73 square metres of body surface area.

Results in Normal Subjects

The results show a marked decrease in urine volume and in sodium and potassium excretion in all of these subjects, with a 10 to 40% fall in creatinine clearance in four (Fig. 8). These findings confirm those of Bock[58] and Peart.[59, 60] But a marked decrease in sodium and potassium excretion can occur without any change in creatinine clearance, as observed in the two other subjects. This is especially clear in subject R.L., in whom marked sodium and potassium retention with persistent lowering of the urinary Na/K ratio occurred without any significant change in creatinine clearance. In this subject, the increase in urinary aldosterone was 11 times above control level and was very rapid, occurring within the first four hours of the angiotensin infusion (Fig. 9).

Results in Hypertensive Patients

The angiotensin infusion given at a hypertensive rate (increase of diastolic pressure of 18 mm. Hg above control level) in patient M.L. resulted in a

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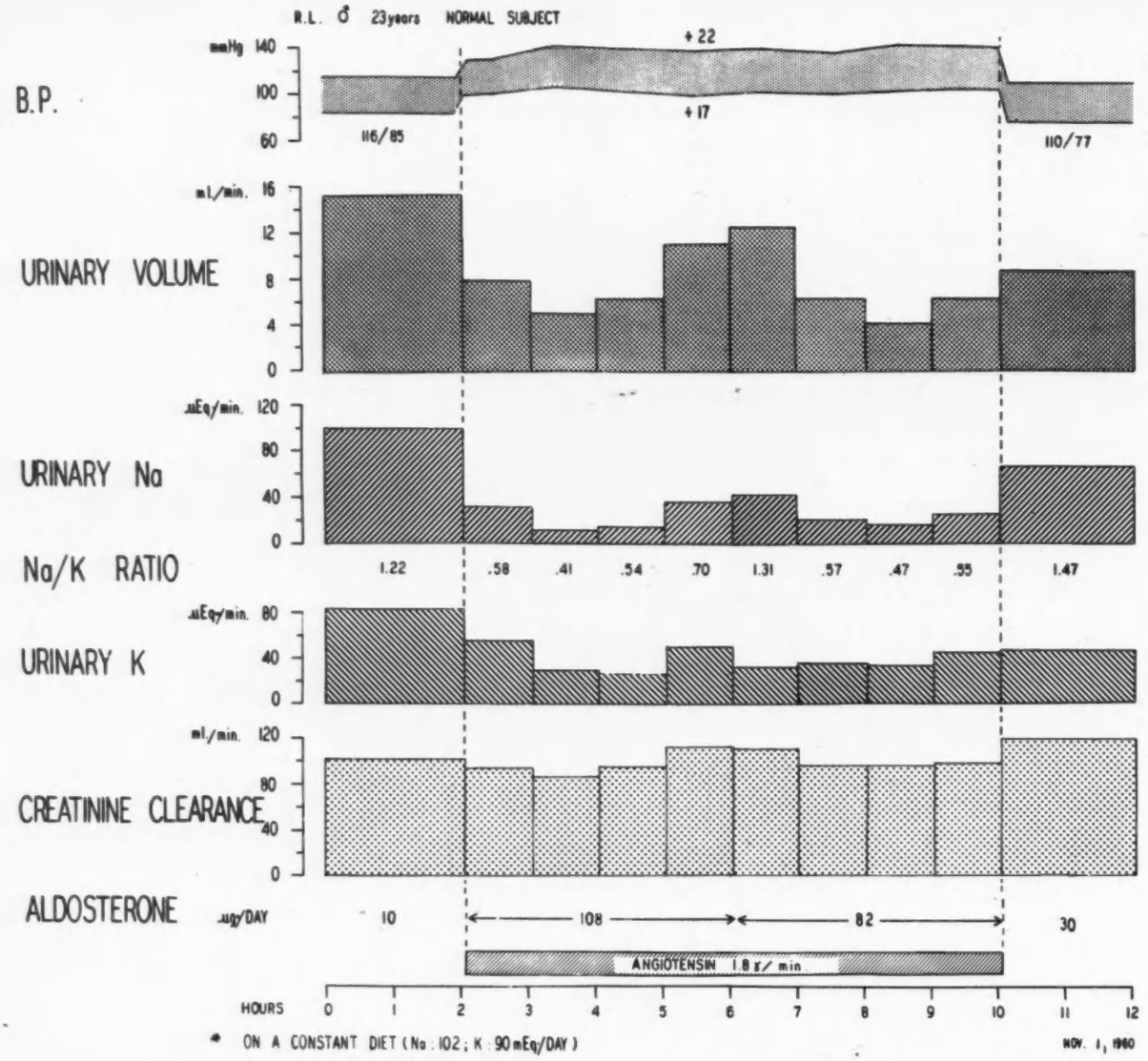

Fig. 9.—Effects of angiotensin infusion (1.8 μg./min. for eight hours), given at a rate productive of hypertensive level to a normal subject (R.L.), on the urinary volume, sodium, Na/K ratio, potassium, creatinine clearance and aldosterone. The stimulation of aldosterone is very rapid, rising to almost 11 times its control value during the first four hours of infusion. This is accompanied by marked sodium and potassium retention. The effect on creatinine clearance is quite slight.

progressive natriuresis to double the pre-control excretion and was followed by a very marked sodium retention. This progressive increase in sodium was accompanied by a rise in Na/K ratio from 1.8 to 3.59 and an increase in kaliuresis. The creatinine clearance showed a 10% increase above control levels (Fig. 10). More experiments of this design are needed in order to find out whether this rise in glomerular filtration rate is the common response of hypertensive patients to angiotensin infusion, as also observed by Peart,[60] and whether it can be the cause of the increased natriuresis.

(2) *Effects of Angiotensin on Urinary Electrolytes, Aldosterone and Other Corticosteroids*

These angiotensin infusions were given for periods of five to 14 hours. Twelve hypertensive infusions, given at a rate to produce a steady increase in diastolic pressure of 15 to 35 mm. Hg above control levels, were administered to 11 normal subjects, and seven infusions to six patients with benign essential hypertension. In addition, four angiotensin infusions given at a sub-hypertensive rate for three to eight hours were administered to three normal subjects and to one patient with essential hypertension.

TABLE III.
EFFECTS OF INTRAVENOUS VALINE-5 ANGIOTENSIN II INFUSIONS* IN NORMAL SUBJECTS†

		Aldosterone‡ (μg./day)			
		Day 1	Day 2		Day 3
Patients	Dose of angiotensin	Control	Angiotensin infusion	Post-Angiotensin infusion	Control
J.M.	2 mg./14 hrs.	14	52	69	68
R.A. (1)	3.1 mg./7 hrs.	10	14	47	
(2)	3.4 mg./13 hrs.	11	105	98	28
F.M.	1.2 mg./8 hrs.	19	32	42	23
J.-P. D.	0.9 mg./7 hrs.	5	36	27	16
H.N.	0.9 mg./12 hrs.	23	84	29	25
G.P.	0.52 mg./5 hrs.	28	138	39	44
J.-L. B.	1.03 mg./5.4 hrs.	24	107	62	25
A.L.	1.01 mg./5.5 hrs.	28	120	57	33
M.L.	1.0 mg./8 hrs.	18	90	35	11
R.L.	0.85 mg./8 hrs.	10	95	30	12

*Increase of 20-35 mm.Hg in diastolic pressure.
†On fixed Na and K intake (102 and 90 mEq./day, respectively).
‡Nowaczynski, Koiw and Genest's procedure.

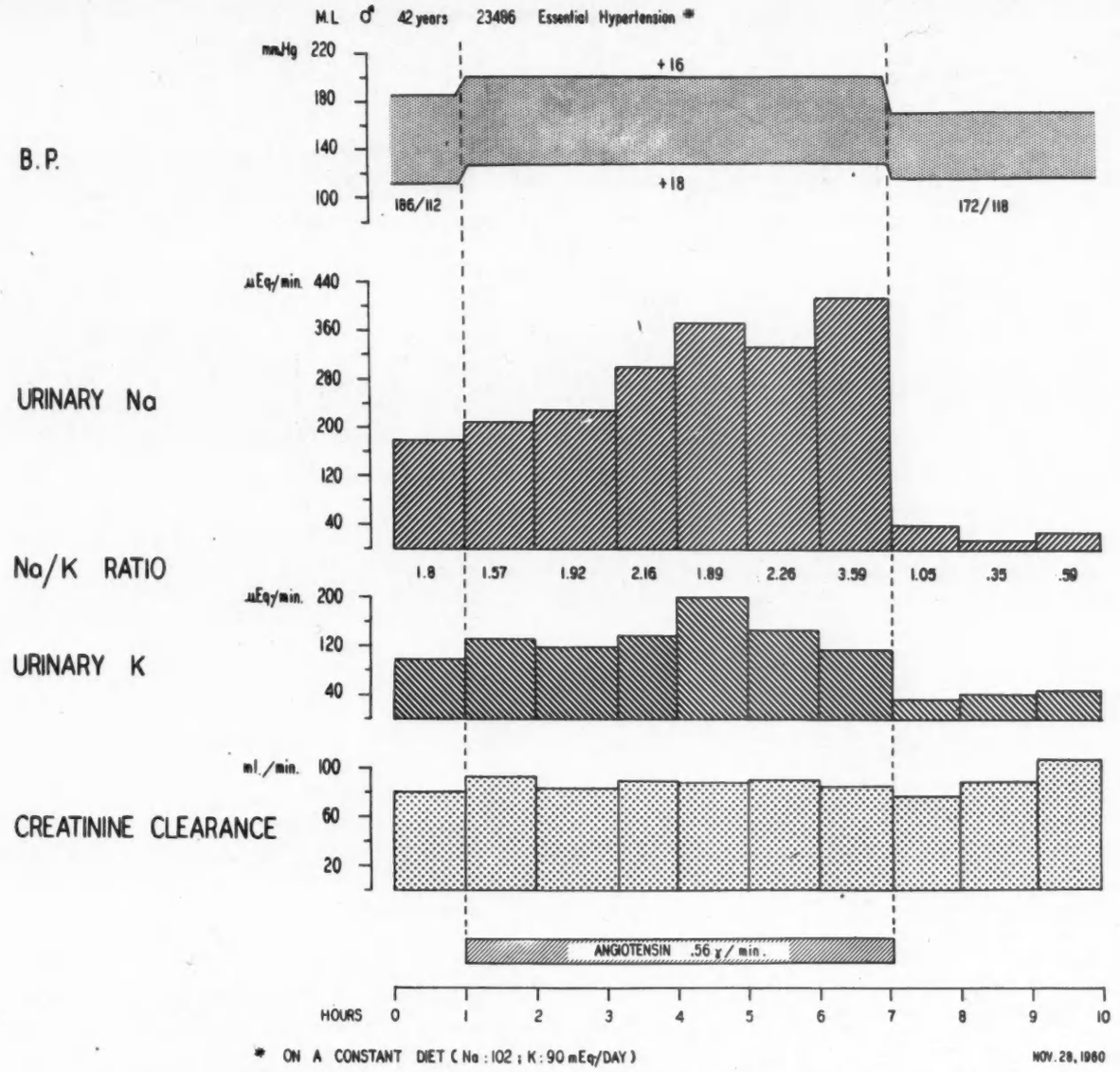

Fig. 10.—Effect of angiotensin infusion (0.56 μg./min. for six hours), given at a rate productive of a hypertensive level in patient (M.L.) with essential hypertension, on urinary sodium, Na/K ratio, potassium and creatinine clearance. There is a progressive and very marked increase in sodium excretion coinciding with a 10% rise in glomerular filtration rate, measured approximately by the creatinine clearance (corrected to 1.73 square metre of body surface area, as in all other experiments).

Results in Normal Subjects

In all normal subjects studied, infusions of angiotensin given at a rate productive of hypertension were always accompanied or followed by a 2.5- to 11-fold increase in urinary aldosterone excretion (Table III) and by a parallel rise in its reduced metabolite, pregnane-3α,18,21-triol, 11,20-dione (also called tetrahydro-aldosterone). This increase persisted in some subjects for one to two days following infusion. It was accompanied by marked sodium retention and a decrease in the urinary Na/K ratio.

In two of four patients extensively studied for urinary excretion of cortisol, cortisone, aldosterone and their "tetrahydro" metabolites (Table IV), there has been a twofold to threefold increase in urinary cortisol and tetrahydro-cortisone. These changes may be within the limit of normal variation of excretion of these two steroids. Nevertheless, a rise of this magnitude in some of the 17-hydroxycorticosteroids, or in the sum of their individual values, appears small in terms of physiological significance in comparison with that caused by the increase in urinary aldosterone during or following the angiotensin infusion.

In subject G. P., with anxiety neurosis, almost complete sodium retention with depression of the urinary Na/K ratio to an extremely low level followed a five-hour hypertensive infusion during which urinary aldosterone rose to 138 μg. per day (Fig. 11).

Comparison of the effect of angiotensin infused at sub-hypertensive (without significant rise in blood pressure during the infusion) and at hypertensive levels in two normal subjects are shown in Figs. 12 and 13. In both subjects, the angiotensin infusions given at sub-hypertensive rates produced a significant degree of aldosteronuria of 57 and 74 μg. per day respectively. These two experiments indicate the extreme sensitivity of the al-

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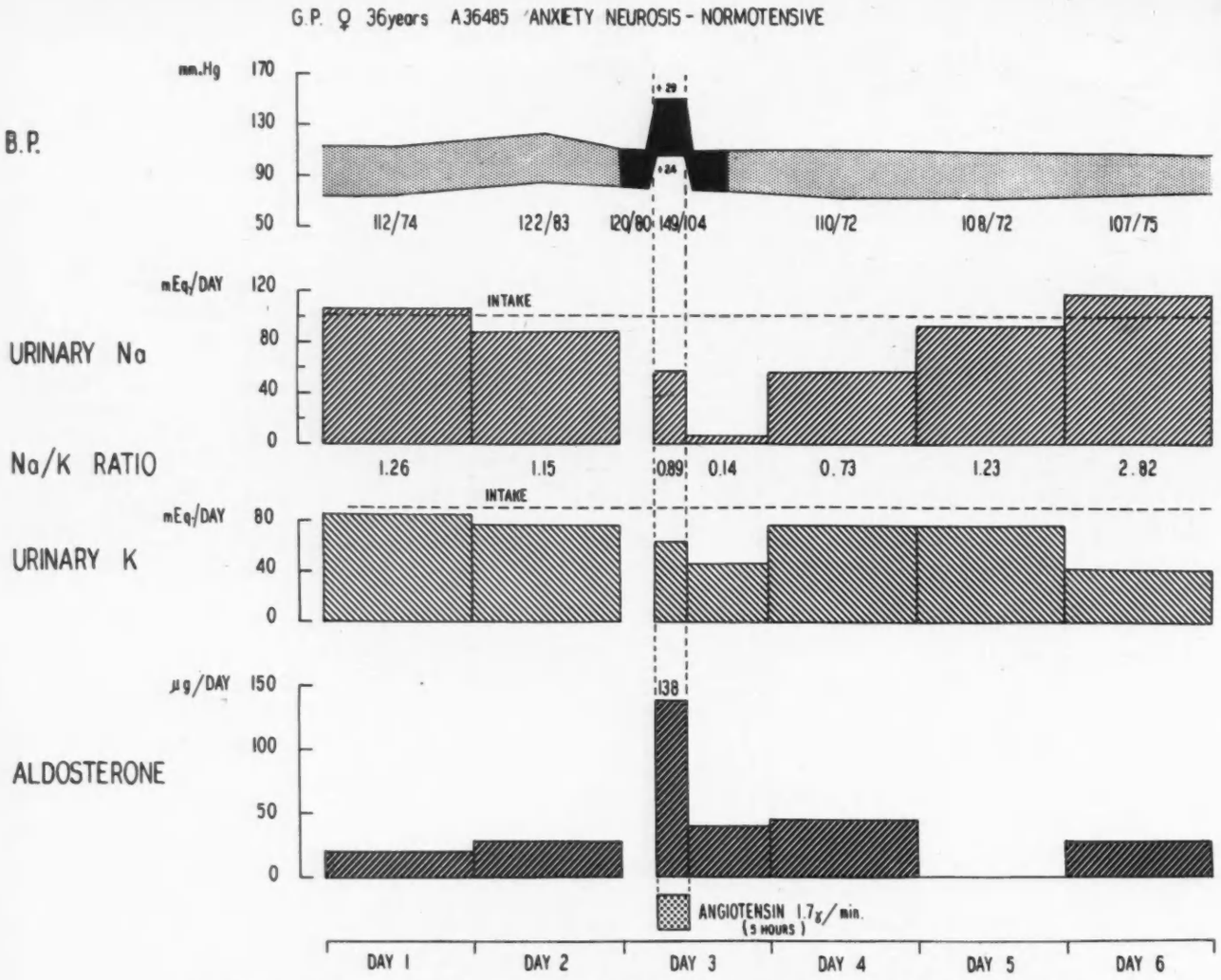

Fig. 11.—Effect of angiotensin infusion, given at a rate productive of a hypertensive level in a normotensive subject (G.P.), on urinary sodium, Na/K ratio, potassium and aldosterone. The striking increase in urinary aldosterone was accompanied and followed by marked sodium retention and a fall in the Na/K ratio.

dosterone response to angiotensin. This response is greatly enhanced when angiotensin is infused at rates productive of hypertension in the two subjects, with subsequent very marked sodium retention and lowering of the Na/K ratio. It is also rapid, as illustrated by subject R.L., whose urinary aldosterone rose immediately during the first four hours of angiotensin infusion, from 10 to 108 mg. per day (Fig. 9). (In this subject, each urine specimen voided during the angiotensin infusion was analyzed for proteinuria. None was detected.)

In order to find out if the increased urinary al-

TABLE IV.—EFFECT OF INTRAVENOUS INFUSIONS OF ANGIOTENSIN IN NORMAL MALE SUBJECTS*

		Urinary Excretion			
	Na†	*Aldosterone*‡	*Tetrahydro-aldosterone*‡	*Cortisol*‡	*Tetrahydro-cortisone*‡
R.A., 22 years					
Day 1—Control	85	11	76	70	1407
Day 2—Angiotensin infusion (3.4 mg./13 hrs.)	31	105	505	218	6792
Post-infusion period	23	98	383	444	2129
Day 3—Control	108	28	138	125	1815
Day 4—Control	78	19	65	180	803
J.M., 26 years					
Day 1—Control	39	14	195	210	790
Day 2—Angiotensin infusion (2 mg./13.6 hrs.)	14	52	336	248	1357
Post-infusion period	12	69	595	102	2358
Day 3—Control	35	68	226	193	3404

*On a fixed Na and K intake (102 and 90 mEq./day, respectively).
†mEq./day
‡Micrograms/day.
No significant change in potassium, cortisone and tetrahydro-cortisol.

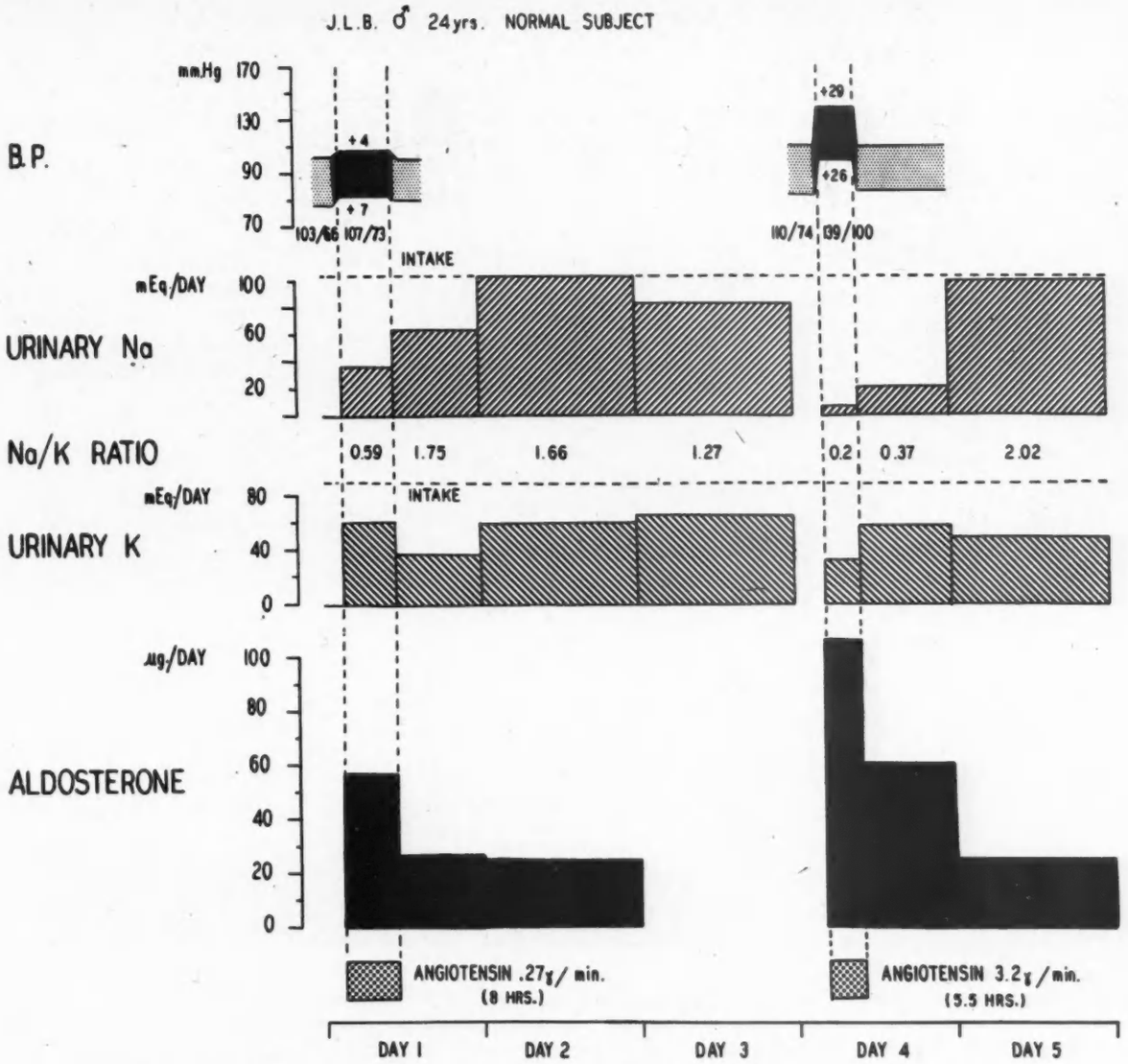

Fig. 12.—Effect of angiotensin infusions, given to a normal subject (J.L.B.) both at "sub-hypertensive" (0.27 µg./min. for 8 hours) and at "hypertensive" rates (3.2 µg./min. for 5.5 hours), on urinary sodium, Na/K ratio, potassium and aldosterone. Even when angiotensin is administered at sub-hypertensive level, there is a significant stimulation of aldosterone with marked sodium retention and a fall in the Na/K ratio. These effects are even more marked when angiotensin is infused at hypertensive rate.

dosterone was the result of the stress of the infusion experiment or the consequence of the artificially induced hypertensive state, control infusions of 5% glucose, adrenaline, noradrenaline* and phenylephrine† were administered for periods of eight hours in several normal subjects. Control 5% glucose infusions in eight normal subjects and three patients with benign essential hypertension did not produce any significant change in urinary aldosterone during or following the infusion.

Phenylephrine infusions were accompanied by a very pronounced natriuresis and a twofold fall in urinary aldosterone in the two subjects studied. Laragh and co-workers[61] have obtained a similar decrease in aldosterone secretion rate accompanied by natriuresis in two subjects given phenylephrine intramuscularly.

In a 23-year-old subject, G.T., who was given phenylephrine infusion at a rate during which the diastolic pressure was maintained at 30 mm. Hg above control levels, the urinary sodium was increased almost fourfold above control levels, while urinary aldosterone decreased from 32 to 11 µg. per day (Fig. 14). In subject R.A., the comparison between the results of the noradrenaline and angiotensin infusions is illustrated in Fig. 15. This subject responded to the noradrenaline infusion by a twofold rise in urinary aldosterone, accompanied by a threefold increase in urinary sodium and a slight increase in the sum of the 17-hydroxycorticosteroids individually measured. The urinary Na/K ratio increased from 1.04 to 3.84 during the noradrenaline infusions. This is the only instance in seven experiments in which urinary aldosterone increased. This rise was very modest in comparison with that obtained during and after a similar hypertensive infusion of angiotensin.

In 1956, Venning[62] and co-workers observed an increase in urinary aldosterone during emotional stresses. Similar findings were obtained by us in

*Levophed, Winthrop.
†Neo-synephrine, Winthrop.

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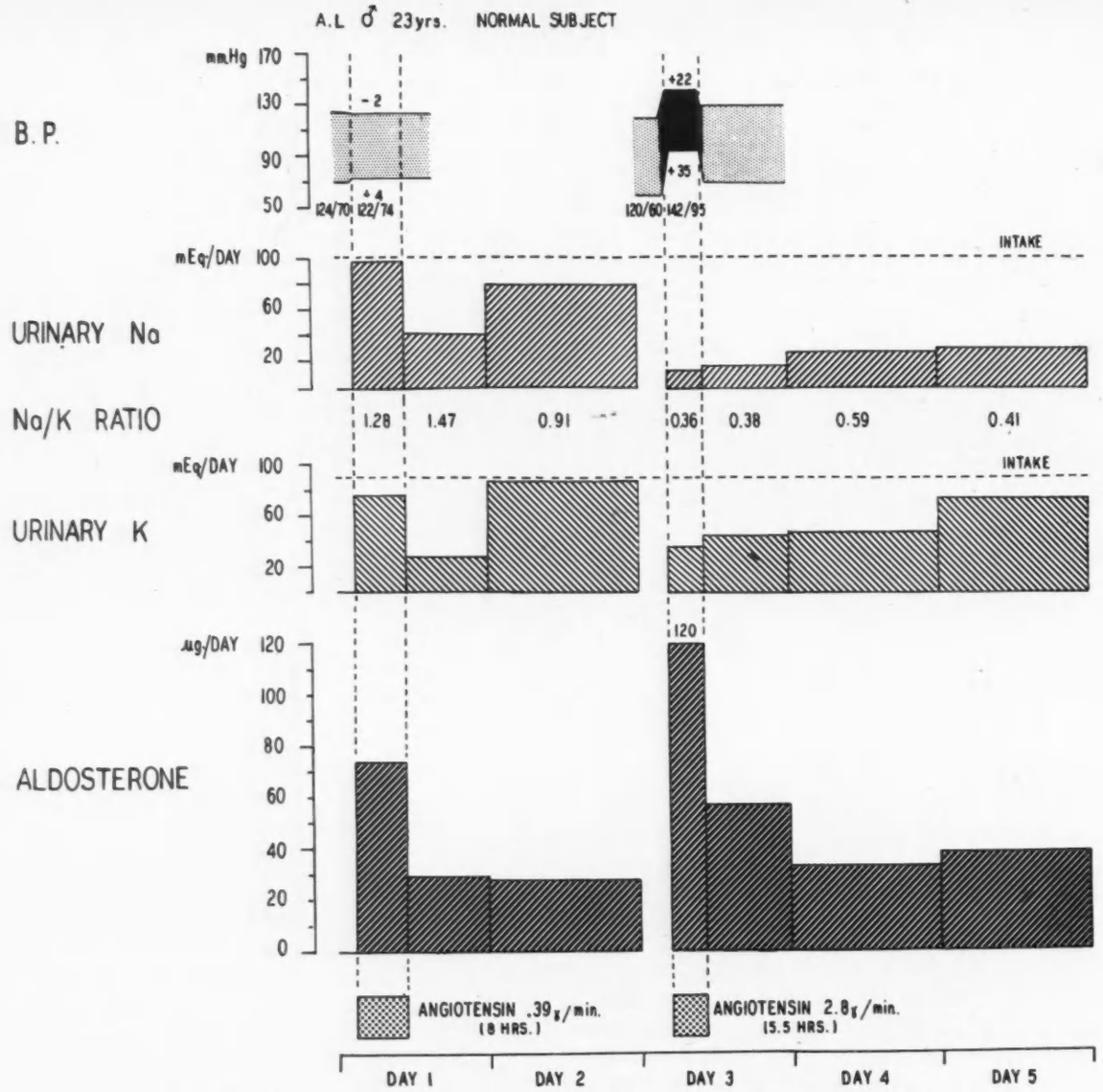

Fig. 13.—Effect of angiotensin infusion, given to a normal subject (A.L.), both at "sub-hypertensive" (0.39 µg./min. for 8 hours) and at "hypertensive" rates (2.8 µg./min. for 5.5 hours), on urinary sodium, Na/K ratio, potassium and aldosterone. When angiotensin was infused at sub-hypertensive rate in this subject, there was little effect on urinary sodium, although there was a twofold increase in aldosterone. Otherwise the changes observed in this subject are similar to those seen in Fig. 12.

patients with anxiety states.[63] Since there were reports from other groups[64] that stresses and anxiety states were also accompanied by an increase in urinary catecholamines, we explored the possibility that high aldosterone excretion during stress or anxiety states could be mediated through adrenaline or noradrenaline. Results reported in 1958 from three normotensive subjects and three patients with benign essential hypertension show that there is essentially no change in urinary aldosterone excretion during infusions of adrenaline at a rate which produces an average increase of 29 pulsations per minute (range 14 to 40) or of noradrenaline at a rate sufficient to produce a slight increase in systolic (mean: 25, range: 12 to 41 mm. Hg) and diastolic (mean: 15, range: 7 to 24 mm. Hg) blood pressures and an average decrease of 11 pulsations per minute (range 5 to 16).[65] These findings were recently confirmed by Laragh and co-workers,[61] who could not find any consistent or significant changes in aldosterone secretion rate in several experiments with adrenaline and noradrenaline infusions.

Results in Benign Hypertensive Patients

In all patients in whom angiotensin was administered at a rate sufficient to produce a significant and stable increase of 15 to 35 mm. Hg in diastolic pressure above control levels, there was very marked natriuresis with a simultaneous increase in urinary Na/K ratio. Although a considerable rise in urinary aldosterone excretion was observed, as in normal subjects, this increase in sodium excretion and in Na/K ratio constitutes a fundamental difference in the response of hypertensive patients to angiotensin infusions as compared with normal subjects.

In patient M.H. with benign essential hypertension, angiotensin infused at a rate productive of hypertension (increase of 16 mm. Hg in diastolic

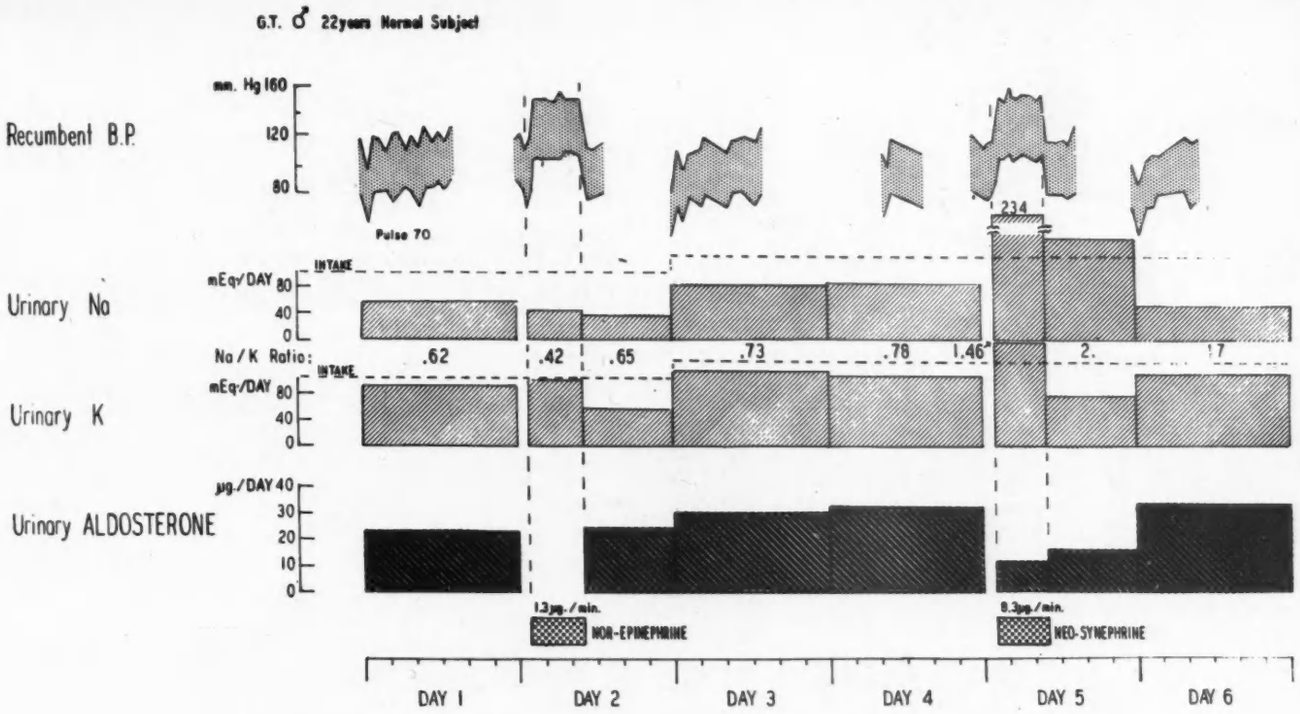

Fig. 14.—Comparative effects of noradrenaline (1.3 µg./min. for eight hours) and of phenylephrine (8.3 µg./min. for eight hours) infusions, given at a rate productive of a hypertensive level (increase of 30 mm. Hg diastolic pressure) in a normal subject (G.T.), on urinary sodium, Na/K ratio, potassium and aldosterone.[57, 71] Unfortunately, the urine collection during the noradrenaline infusion was lost before the aldosterone determination was completed. During the phenylephrine infusion there was a significant fall in the urinary aldosterone accompanied by very marked natriuresis and a rise in Na/K ratio and potassium excretion.

pressure above control levels) resulted in a very significant increase in urinary aldosterone which persisted during the immediate night-period after cessation of the angiotensin infusion (Fig. 16). This was accompanied by very marked natriuresis and a rise in the urinary Na/K ratio.

Patient J.B. with benign essential hypertension received angiotensin infusions at rates productive of sub-hypertensive and hypertensive levels (Fig. 17). During the "sub-hypertensive" infusion, urinary sodium rose threefold with a marked rise in Na/K ratio, despite a twofold increase in urinary aldosterone. Five days later, angiotensin infused at "hypertensive" rates (increase of 33 mm. Hg in diastolic pressure above control levels) for five hours produced an even more marked natriuresis and rise in Na/K ratio, despite a threefold increase in urinary aldosterone. The very significant natriuresis was followed during the night-period by a still greater degree of aldosteronuria to 136 µg. per day, accompanied this time by severe sodium retention and a fall in the Na/K ratio.

F. *Blood Angiotensinemia*

When the preliminary results of the specific and very marked stimulation of aldosterone by angiotensin became known in the middle of 1959, we decided to enter the field of blood polypeptides in an attempt to obtain a satisfactory method of fractionation of pressor polypeptides for isolation of angiotensin. Such a method, which modifies in several ways the procedure of Paladini *et al.*[66] because of its insufficient sensitivity and specificity, has been devised in the last year and a half by Boucher and Biron in our laboratory.[67] This procedure involves the immediate precipitation of 100 to 300 ml. of blood with ethanol, ether extraction of the filtrate and successive purification of the aqueous phase, first by column chromatography on cationic Dowex resin, then by paper chromatography and the detection and measurement of angiotensin by a rat assay for pressor activity. (The details of this procedure will be published in the March 1961 issue of the *Canadian Journal of Biochemistry and Physiology*.[67])

TABLE V.

SIMILARITIES BETWEEN "ANGIOTENSIN" ISOLATED FROM HUMAN BLOOD AND STANDARD VALINE-5 ANGIOTENSIN II, ASPARTIC β-AMIDE

1. Identical Rf values in paper chromatographic systems:
   (a) Sec. Butanol: Isopropanol : Water : Phosphate Buffer pH 8 = 7:7:5:2 (*Rf 0.55*)
   (b) Butanol:Acetic Acid:Water = 4:1:5 (*Rf 0.35*)
2. Identical migration in paper electrophoresis
   Conditions: pH 6.2, ammonium acetate buffer, 5V/CM, 5 hrs.
3. Identical pressor response curve in the rat bioassay.
4. Quantitative recovery of added angiotensin to blood with the same characteristics as mentioned in 1, 2 and 3.
5. The angiotensin isolated from blood during infusion of this substance shows the same characteristics as the material isolated from hypertensive patients (see above 1, 2 and 3).
6. The angiotensin isolated from human serum after its incubation with renal tissue from a patient with unilateral renal hypertension* shows the same characteristics as the material isolated from hypertensive patients (see above 1, 2 and 3).
7. Inactivated by trypsin.

*This patient had a complete occlusion of the right renal artery with a clinical and biochemical syndrome simulating primary aldosteronism.

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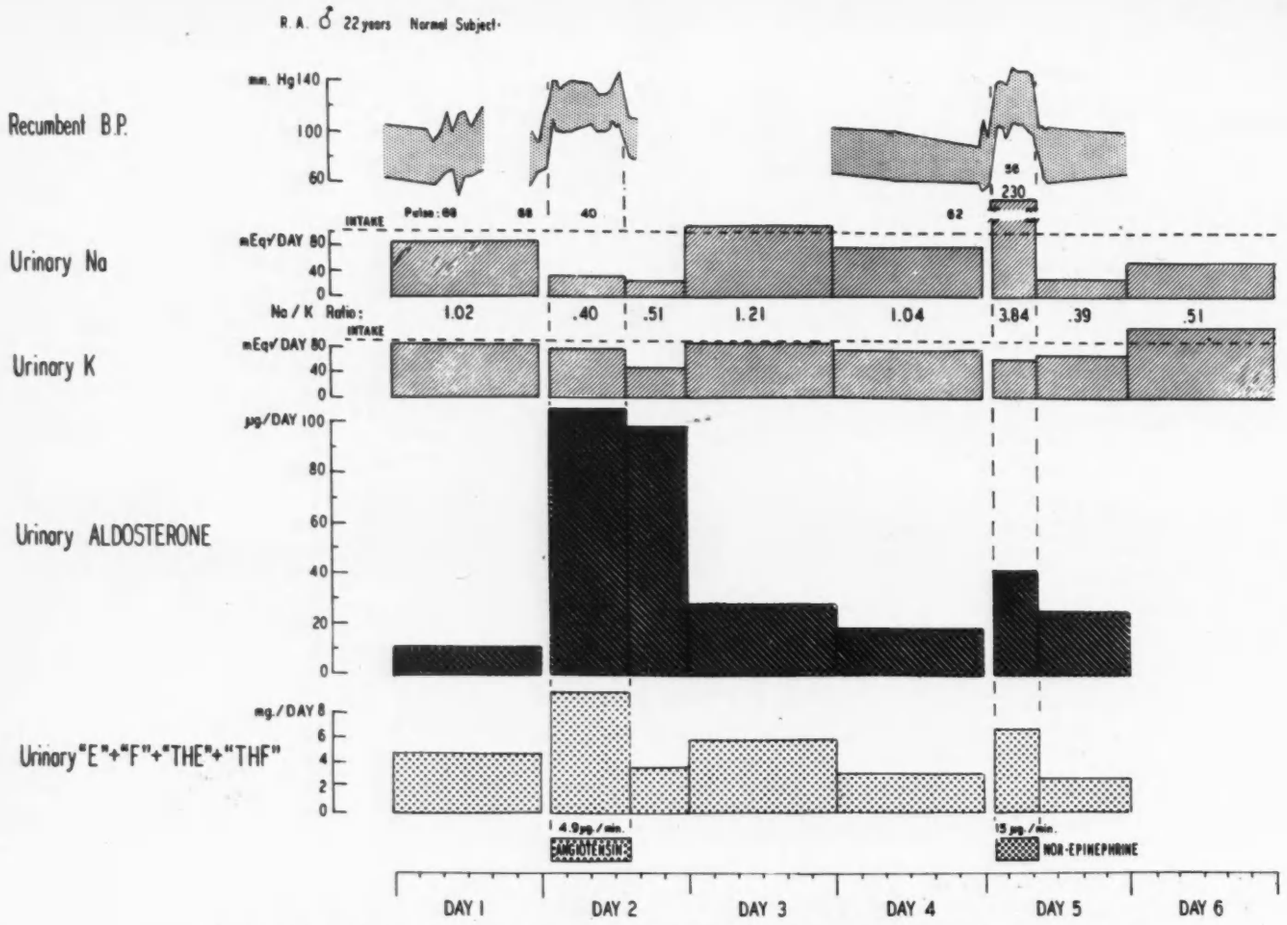

Fig. 15.—Comparative effect of angiotensin (4.9 µg./min. for 15 hours) and of noradrenaline infusions (15 µg./min. for eight hours), given to a normal subject (R.A.), both at a rate productive of a hypertensive level (increase of 30 mm. Hg diastolic pressure above control level), on pulse rate, urinary sodium, Na/K ratio, potassium, aldosterone and on the sum of the urinary corticosteroids, cortisone ("E"), cortisol ("F") and their tetrahydro derivatives measured individually.[67, 71] The tenfold increase in urinary aldosterone during and after the angiotensin infusion is most striking, compared with the twofold rise during noradrenaline infusion. This was the only instance in seven experiments where urinary aldosterone increased significantly during noradrenaline infusion. Despite this slight increase, there was a very marked natriuresis and rise in Na/K ratio.

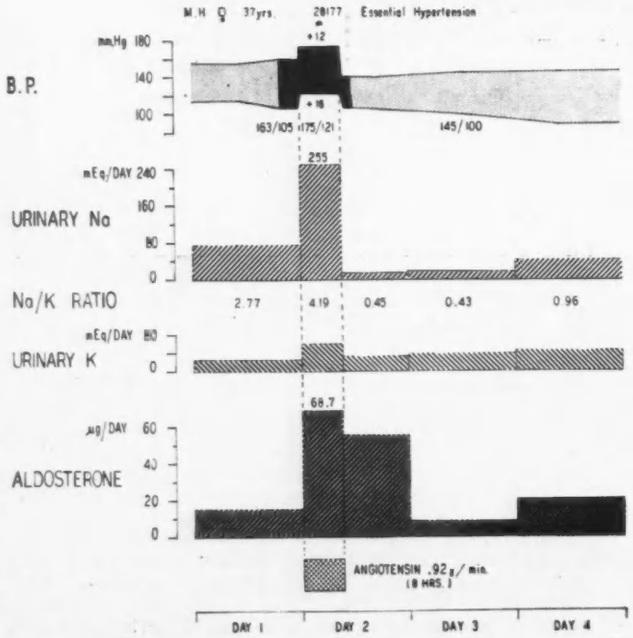

Fig. 16.—Effects of angiotensin infusion (0.9 µg./min. for eight hours), given at a rate productive of a hypertensive level to a patient (M.H.) with benign essential hypertension, on urinary sodium, Na/K ratio, potassium and aldosterone. Despite the very marked increase in urinary aldosterone, we observe a threefold increase in urinary sodium and a marked rise in Na/K ratio.

This procedure has yielded quantitatively determinable amounts in 13 different experiments. Its accuracy varies from 10 to 20% and its sensitivity is of the order of 5 to 10 mµg. per 100 ml. of blood. The specificity of the method is based on the similarities described in Table V, between the "angiotensin material" isolated from human blood and the standard valine-5 angiotensin II, asparagine.

Infusions of angiotensin were administered to six normal subjects at hypertensive rates and their arterial or venous blood was collected for measurement of angiotensin levels according to our procedure. The results given in Table VI indicate that the arterial blood levels of angiotensin vary markedly from individual to individual, from 34 to over

TABLE VI.
EFFECTIVE ANGIOTENSIN BLOOD LEVELS* IN NORMAL SUBJECTS

Subject	*Rate of administration µg./min.*	*Average increase in diastolic pressure†*	*Blood levels nanograms/100 ml. blood*	
			Arterial	*Venous*
R.A.	6	30	200+	
J.P.B.	2.2	30	36	
J.P.B.	1.6	20		34
E.H.	2.5	31	114	
M.L.	1.9	36	130	
A.L.	3.8	30	34	14
M.L.	5.2	30	204	

*By constant intravenous infusions.
†mm.Hg

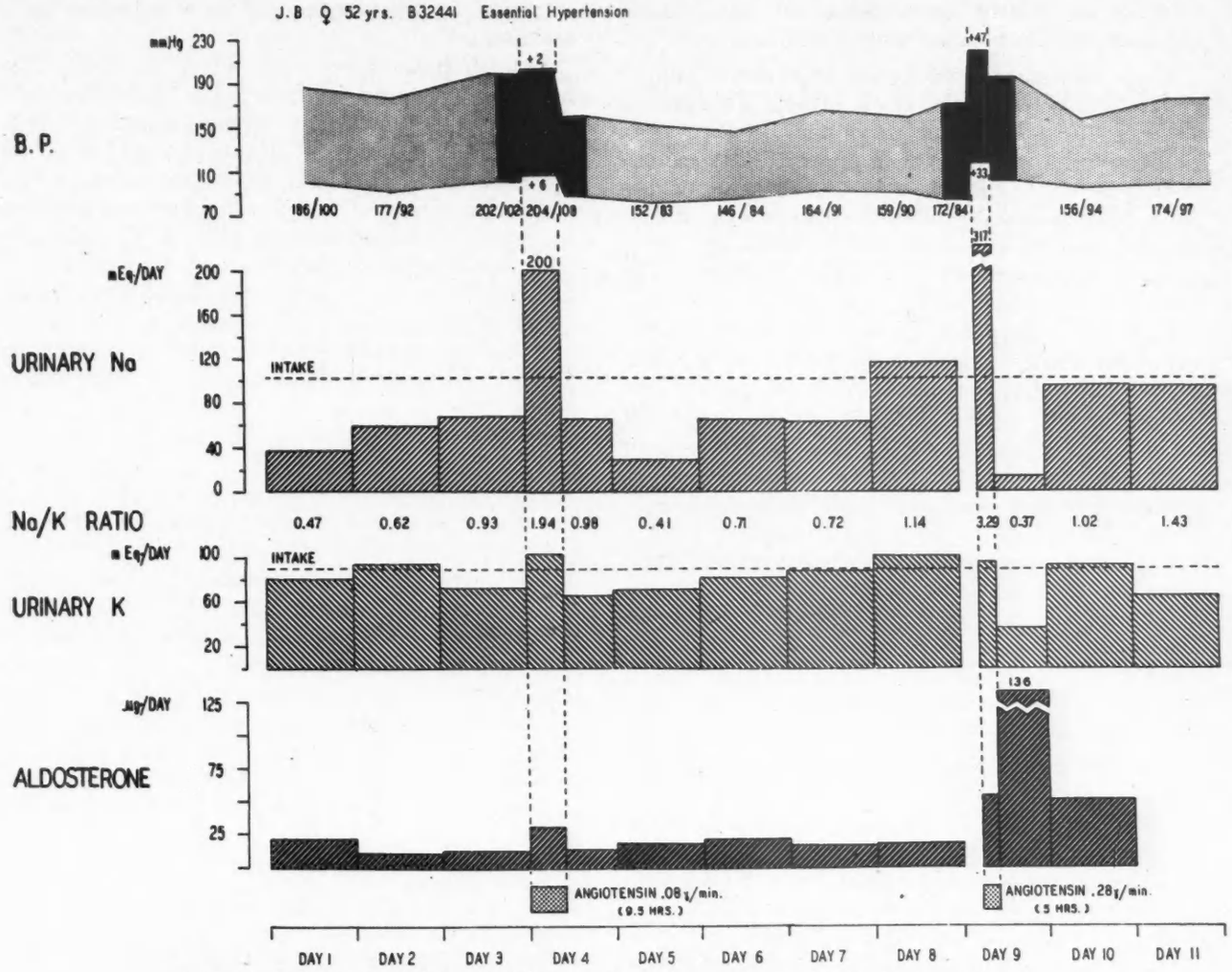

Fig. 17.—Effects of angiotensin infusions given to a patient with benign essential hypertension (J.B.), both at "sub-hypertensive" (0.08 µg./min. for 9.5 hours) and at "hypertensive" rates (0.28 µg./min. for 5 hours), on urinary sodium, Na/K ratio, potassium and aldosterone. In both instances, despite a twofold to threefold increase in urinary aldosterone, there was a greatly increased natriuresis and Na/K ratio. Immediately after the angiotensin infusion, given at hypertensive rate, urinary aldosterone rose to 136 µg./day, with marked sodium retention. This further rise in urinary aldosterone following the infusion appears secondary to the important natriuresis which occurred during the infusion.

200 mµg. per 100 ml. of blood, despite a similar rise in diastolic pressure.[68] The results obtained so far in patients with various types of hypertension, including that of primary aldosteronism, are still too few in number and preliminary to report.

G. *Features of Early Hypertension*

The main features of early benign hypertension in humans are outlined in Table VII. Basically, the outline centres around two main conceptions: (1) that the hypertensive process, at least in the early phase, is essentially a discontinuous one, and (2) that it is profoundly influenced by disturbances in sodium, aldosterone and progesterone regulation or metabolism, and that these disturbances are probably closely linked with liberation of angiotensin by the kidney.

TABLE VII.
MAIN FEATURES OF EARLY BENIGN HYPERTENSION IN HUMANS

1. Asymptomatic
2. Discontinuous process—
   (a) Excessive fluctuations in B.P.

Emotional	factors ↑	Physical rest
Environmental	"	Peace of mind
Maladjustment	"	Sedatives—tranquillizers
High salt intake	"	↓ Low salt diet

   (b) Excessive fluctuations in daily aldosterone excretion
3. Low urinary pregnanetriol/aldosterone ratio
4. Lowering of B.P. by: natriuretic drugs
   aldosterone antagonists
5. Increased tubular rejection of filtered sodium following salt loads
6. Natriuretic response to angiotensin despite increased aldosterone stimulation

DISCUSSION

Since reporting some preliminary results of the specific and strong stimulation of aldosterone by angiotensin in normal subjects at the American Heart Association meeting in Philadelphia in October 1959,[69] cited by Tobian[1, 13] we have presented our detailed findings simultaneously at the meeting of the Canadian Federation of Biological Societies in Winnipeg, June 1960,[70] at the International Symposium on Essential Hypertension in Bern, June 1960,[71] and subsequently at the First International Congress of Endocrinology, in Copenhagen, July 1960.[30] Our work was confirmed in September 1960 by Laragh and co-workers,[61] who have found an

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increase in aldosterone secretion in four normal subjects receiving angiotensin infusions.

These results establish for the first time the direct correlation between the renal pressor mechanism, aldosterone and sodium in human hypertension. They give strong clinical support to the experimental evidence linking the granulations of the renal juxtaglomerular cells to the width of the adrenal zona glomerulosa and sodium regulation, which has been reviewed in detail by Tobian.[1, 13] In brief, this evidence can be summarized as follows. The width of the adrenal zona glomerulosa secreting aldosterone, the granularity of the renal juxtaglomerular cells probably secreting renin and the "renin content" of the kidney vary in a parallel manner. They increase in response to low sodium intake and in all cases where the renal artery pressure is low, such as after total bilateral adrenalectomy or during low-pressure perfusion experiments. On the other hand, they decrease in response to high sodium intake or in response to high renal artery pressure, such as is encountered in renal experimental hypertension, in adrenal regeneration hypertension, after administration of renin or of desoxycorticosterone, and during high-pressure perfusion experiments.

The effect of angiotensin administration in normal subjects appears to be twofold: (1) There is a hemodynamic effect with a fall in glomerular filtration rate and the filtered load of water, sodium, chloride and potassium, with subsequent reduction in their excretion. The fall in filtration rate is seen almost only when angiotensin is infused at a rate which produces a significant rise in blood pressure.[59, 60] This effect on filtration rate has been shown by Bock[58] to be transitory, since the glomerular filtration rate often returns to its control level even during the period of infusion. (2) There is a direct effect on tubular reabsorption of sodium and water, either *per se* or more probably through an increase in aldosterone secretion, as the present experiments strongly indicate. The facts (a) that the increase in urinary aldosterone is very rapid in some subjects, (b) that the increase is present during infusions given at sub-hypertensive levels, and (c) that sodium retention appears independent of any significant reduction in glomerular filtration rate in some subjects, give greater support to the latter concept. On the other hand, the natriuresis seen in hypertensive patients in response to angiotensin is probably due to the increase in glomerular filtration rate which overcomes the tubular effect of the increased aldosterone.

The stimulatory effect of angiotensin on aldosterone is quite marked and specific. It is not indeed the result of the induced hypertensive state *per se*, since it is also produced by infusions given at a rate productive of sub-hypertensive levels of angiotensin and is not encountered with similar infusions of phenylephrine and noradrenaline (with one exception in seven experiments), although significant increases in blood pressure were achieved in all instances.

Our findings agree with those of Deane and Masson,[12] recently confirmed by Hartroft *et al.*[18] and by Gross,[72] who have demonstrated that renin administration produces a marked and rapid increase in the width of the zona glomerulosa in rats.

Another aspect of these studies is given emphasis by the recent experiments of Hilton[73] using *in vitro* perfusion of the adrenal glands of dogs. Hilton has demonstrated that vasopressin stimulates cortisol secretion but not that of aldosterone. Since vasopressin is closely related chemically to angiotensin, it is of interest to know that these two related polypeptides can specifically and differentially stimulate the secretion of the two main adrenal corticosteroid hormones.

With the help of the procedure of Boucher *et al.* for the measurement of angiotensin after its isolation to a high degree of purity, it will be of decided interest to carry out serial determinations of blood angiotensin, urinary aldosterone, "tetrahydro-aldosterone" and pregnanetriol in patients with various types and stages of arterial hypertension. It is our hope that the results obtained so far will contribute significantly to a better and more complete understanding of the relationship of the renal, adrenal and sodium factors in the pathogenesis of this disease.

SUMMARY AND CONCLUSION

We have described the history of a research problem pursued continuously during the last 12 years and based on the hypothesis that there is an important relationship between the adrenal cortex, sodium and the kidney in the genesis of human hypertension. Our findings permit the following conclusions: (1) There are definite abnormalities of adrenocortical activity in human hypertension as shown by the disturbances in urinary aldosterone, pregnanetriol and pregnanetriol/aldosterone ratio. (2) Angiotensin II infusions stimulate specifically urinary aldosterone both in normal and hypertensive subjects. (3) Whereas this increased aldosterone level during angiotensin infusions is accompanied by marked sodium retention and lowering of the Na/K ratio in normal subjects, the urinary sodium and the Na/K ratio increase markedly in patients with benign essential hypertension. This basic difference in response to angiotensin between normal subjects and hypertensive patients points to a fundamental problem which requires solution in order to obtain a better understanding of the disease. The relative or absolute excess of aldosterone over progesterone secretion may be the important adrenal disturbance among the basic factors involved in the pathogenesis of arterial hypertension. This disturbance is definitely linked with angiotensin and sodium regulation.

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EXPERIENCES WITH ANGIOGRAPHY BY THE PERCUTANEOUS CATHETER SPRING GUIDE TECHNIQUE*

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DURING RECENT years some of the most important advances in diagnostic radiology have been in the field of angiography. The most spectacular have perhaps been with angiocardiography, but this is a procedure largely confined to institutions possessing elaborate apparatus used by special cardiovascular units. Other simpler forms of angiography, such as aortic and peripheral arteriography, may nevertheless lend themselves to more widespread application. Experiences with an angiographic technique which has become widely accepted since its original description by Seldinger in 1953,[1] and which has many applications, will be reported.

A safe, accurate and simple method of angiography, allowing contrast medium to be injected close to the site of suspected disease without discomfort to the patient, is the ideal to be aimed at. These criteria do not universally apply to translumbar aortography. While one occasionally still finds reference to series of such examinations performed without serious complications, the growing literature concerning such complications cannot be ignored.[2-7] In experienced hands translumbar aortography is relatively simple to perform, but it is not devoid of discomfort to the patient unless done under general anesthesia. Moreover, it is not easy to place the tip of the needle in precisely the desired position for accurate injection.

Because of the shortcomings of direct puncture into the aorta, indirect catheter techniques by way of peripheral arteries were devised, but the early methods, in which tubing was threaded through the lumen of the puncturing needle, had the disadvantage that the needle had necessarily to have a large external diameter. Seldinger overcame this by his catheter and guide-wire technique, which enables polyethylene tubing of the same external diameter as the cannula to be introduced to any desired level by simple percutaneous puncture.

Modifications of Seldinger's method have been evolved subsequently, enabling it to be applied to almost every part of the body including the heart[8] and cerebral circulation.[9]

In certain cases of angiography of the limbs and in some cases of venous angiography also, we have found the catheter technique to have distinct advantages in permitting contrast medium to be injected close to a suspected lesion.

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METHOD

Small details and variations of technique and apparatus are not within the scope of this paper.

Basic Technique

The method we have employed is virtually that described by Seldinger in 1953. In its essentials it consists in the insertion of a concentric inner needle and outer cannula into a peripheral artery. When the cannula is well in place and the central needle withdrawn, a long flexible wire coil similar to a wound metal music string is passed through into the lumen of the artery. The cannula is then withdrawn over the guide wire, leaving the first inch or two of the guide alone in the artery. Polyethylene tubing, which has been cut to the requisite length, trimmed, and attached to a special tap for final connection to the Luer-Lok injecting syringe, is next slid, sleeve-wise, over the guide to the skin surface. The catheter is then gripped firmly on the guide to prevent further slipping between them, and both are advanced gently together. Once in the lumen, the relative positions of the tips of the guide and catheter are adjusted by predetermined measurement so that the flexible tip of the guide is a little in advance of the catheter tip. They are gripped firmly together again and gently advanced until in the desired position. The guide wire is longer than the catheter and its free end is thus by this time projecting from the outer end of the catheter. The wire can therefore be finally withdrawn back through the catheter, leaving the latter in place and free for injection of radio-opaque material.

The exact site of the tip of the catheter may be determined by fairly rapidly injecting approximately 5 c.c. of contrast medium and taking a check radiograph during injection. Alternatively, a Kifa radio-opaque catheter may be used and is of particular value in selective injection of any given branch artery, though we have not used such a catheter to date. Visualization of a segment of a main vessel, from which several branches to be demonstrated are arising, has been our main object. For this a preliminary injection of contrast medium is essential and this injection automatically opacifies the catheter. Nevertheless, as our experience and needs extend to selective angiography of branch arteries, we shall use radio-opaque catheters.

No general anesthetic is required for the procedure, but suitable premedication of the patient and local anesthesia of the percutaneous puncture site are indicated.

Once the preliminary 5 c.c. injection and the test film have shown the catheter tip to be properly in position, 30 c.c. of 60% Renografin, 50% Hypaque or equivalent contrast medium is rapidly injected manually and serial films are taken, the series being started just before the end of injection.

After injection the catheter is flushed through with saline and the stop-cock attached to it is

turned into the closed position while the films are developed. If no further films are required the catheter is withdrawn and the site of percutaneous puncture is manually compressed for at least five minutes, and longer in hypertensive patients.

Gregg[10] advocates injection of 5000 to 10,000 units of heparin and 50 mg. of tolazoline (Priscoline) in 20 ml. of saline before catheter removal. He believes that it lessens the chance of distal arterial thrombosis and promotes peripheral vasodilatation.

Additional Features of Technique

A large proportion of our patients were elderly and had arteriosclerotic changes; we have in consequence occasionally encountered difficulty in advancing the catheter and guide into the aorta because of marked tortuosity of the iliac arteries. One patient was encountered in whom it was impossible to reach the aorta via either iliac artery and the procedure was abandoned; in the next patient it was impossible to reach the aorta from one femoral artery, but it was reached from the other. The needles and guide wires are manufactured in large and small sizes; following these experiences, the fine flexible guide wire has been used on several occasions and has passed readily along tortuous iliac arteries after the standard-sized guide has failed. The larger polyethylene tubing does not fit this smaller guide wire quite as snugly, but with suitable moulding can still be easily used so that rapid injection is not impaired. Several examinations have now been successfully performed in this way, which might otherwise have been failures.

As already noted, we have not extended our examinations to selective angiography of any particular branch artery, but selective injection has its advantages in that excellent arteriograms are achieved using small doses of contrast medium.[11] For example, the right subclavian artery abnormality shown in Figs. 5a and 5b would probably have been much better demonstrated by selective injection of the artery; nevertheless we wished to show the general anatomy in the region first, and having done so and demonstrated the lesion, we did not feel justified in prolonging the procedure by attempting selective catheterization.

The value of injecting contrast medium close to the site of certain suspected peripheral vascular lesions is well illustrated by Figs. 3b and 3c.

We have also used this method in cases of suspected superior vena cava obstruction, as it permits injection close to or directly into the superior vena cava. This makes timing easier to judge and prevents dissipation of dye into other dilated veins in the region; it also ensures that the site of injection is far enough from the puncture to avoid extravasation into the soft tissues close to the puncture site. Furthermore, the catheter is flexible and cannot be accidentally dislodged by movement; the patient can thus be moved around for different radiographic projections without discomfort or danger, and without inconvenience to the operator during injection.

Fig. 1.—Renal hypertension. Stenosis of left renal artery (arrow).

MATERIAL

Our own experience is relatively limited, consisting of 23 examinations, 15 of which have been renal angiograms, two peripheral femoral angiograms, five superior vena cavograms, and one injection into the aortic arch.

Renal Angiograms

Of these, eight were carried out for suspected renal hypertension, four for undiagnosed hematuria and three for an abnormality shown on pyelograms.

1. In the hypertensive group, definite unilateral vascular abnormalities were shown on four. All these patients had nephrectomies of the affected kidneys and in three the blood pressure returned to normal limits the same day.

A representative radiograph of one of these patients is shown in Fig. 1. This 53-year-old man was admitted to the otolaryngology service in May 1960 for treatment of chronic sinusitis. While in hospital his blood pressure was found to be 200/110 mm. Hg. Intravenous pyelograms and retrograde pyelograms were normal, but differential sodium studies showed marked diminution in volume and sodium excretion from the left kidney. The renal angiogram showed stenosis of the origin of the left renal artery with poststenotic dilatation. There was also a poor left nephrogram. Left nephrectomy was performed. At the beginning of operation the systolic blood pressure was 220 mm. Hg, but at the conclusion it was 160. The patient made a good postoperative recovery, with a blood pressure in the region of 140/75. Sections of the renal artery

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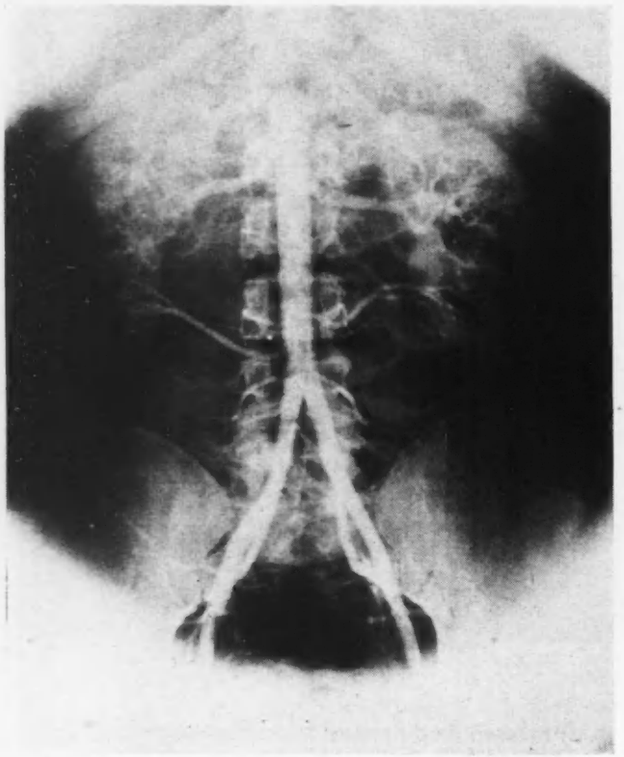


Fig. 2.—Normal renal angiogram of patient with hematuria. Note accessory arteries directly from aorta to lower poles of both kidneys and to midportion of right kidney.

showed focal arteriosclerosis, which had produced stenosis of the lumen.

The fourth patient operated upon showed no significant change in his blood pressure, and he was still hypertensive at the time of discharge.

In another case in the hypertensive group a possible minor plaque-like anomaly of the origin of the right renal artery was demonstrated, but this was not considered sufficient justification for operation. A repeat angiogram performed one year later showed no abnormality, and this second angiogram is included in the group in which no cause was found for the renal hypertension by angiography.

No abnormality was shown on the angiogram in the other three hypertensive patients, and none of them was operated upon.

2. Four renal angiograms were performed because of hematuria in patients whose pyelograms showed no abnormality; likewise no abnormality was shown on any of these angiograms. Fig. 2 is an example of one of these cases and is included because the accessory renal arteries arising directly from the aorta to supply the lower poles of both kidneys are of interest.

3. Of those examinations carried out for abnormal pyelograms, one was performed because of nonfunction of the left kidney after an acute episode of left loin pain. This showed no blood supply to the left kidney, and the final diagnosis was thrombosis of the left renal artery. The patient was not hypertensive, and no operation was performed.

The pyelograms of the other two patients in this group showed space-occupying lesions. The renal angiogram of one showed evidence of a cyst of the right kidney. The angiogram of the other was a failure because of tortuosity of the iliac arteries as already noted, but a subsequent translumbar aortogram showed evidence of a right renal cyst. No operative proof was obtained in either case.

Peripheral Vascular Angiograms

Both these were carried out on the same patient, one preoperatively and the other postoperatively. As noted above, these examinations constitute good examples of the value of injecting contrast medium close to the site of certain suspected peripheral vascular lesions.

The patient was a 40-year-old man who had sustained a gunshot wound in the region of his right calf in 1944. Since then he had noticed tightness in the calf on walking. A routine percutaneous femoral arteriogram with the injection made just below the inguinal ligament vaguely showed an arteriovenous shunt in the calf. The rate of blood flow was nevertheless so rapid that sufficient concentration of dye could not be obtained to show the essential details (Fig. 3a).

Percutaneous catheter angiography was then performed with the tip of the catheter in the popliteal artery at the level of the knee. This very clearly showed a fistula between the peroneal artery and vein with immediate visualization of this vein. There was also dilatation of these vessels and of most of the other vessels in the region (Fig. 3b). Ligation and excision of the fistula were carried out. A recheck postoperative percutaneous catheter angiogram showed disappearance of the fistula and decrease in the number and size of the vessels in the region (Fig. 3c).

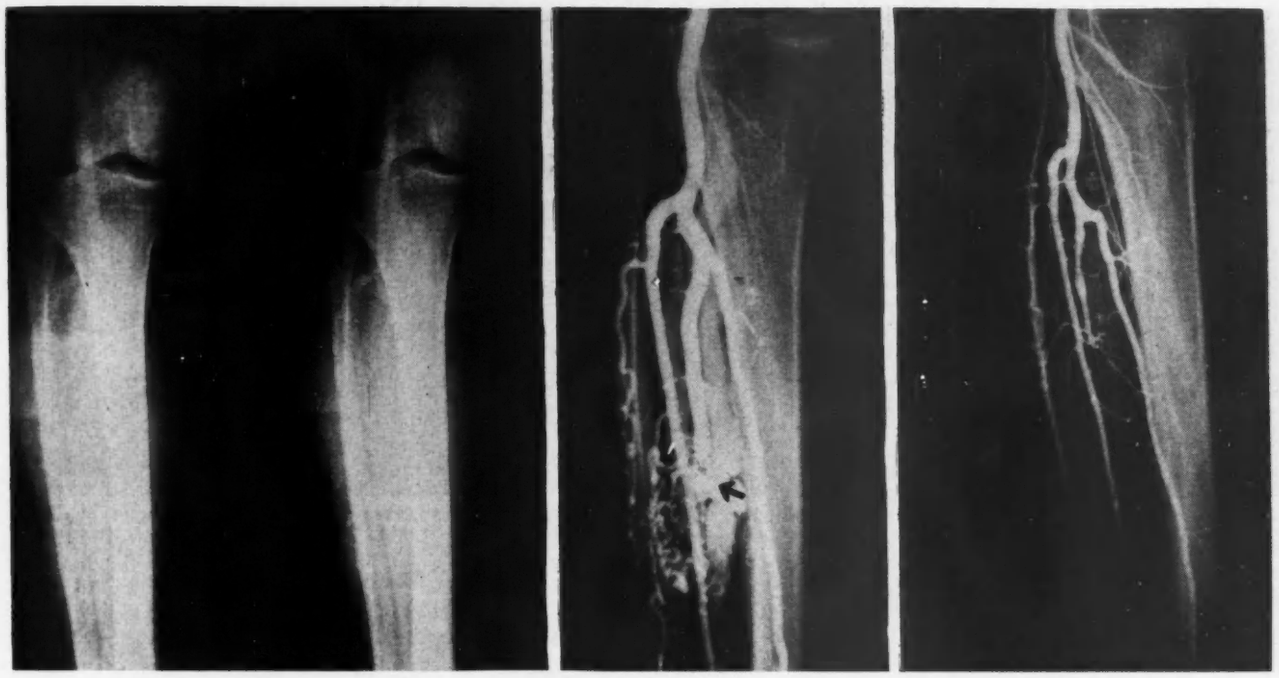
Superior Vena Cavograms

Five examinations were carried out for suspected superior vena caval obstruction. Two were performed on patients with superior mediastinal masses thought to be bronchogenic carcinomas; both showed invasion of the superior vena cava by neoplasm. Fig. 4 is an example of one of these.

Of the other three, one was a patient with arteriosclerotic heart disease and hypertension, the second had chronic bronchitis and emphysema, and the third had clinically diagnosed constrictive pericarditis. No evidence of vena caval obstruction was found in any of these three patients.

Injection into the Aortic Arch

We have performed only one such examination. The patient had suffered severe trauma to his right supraclavicular fossa in 1946. He subsequently had persistent weakness and tingling in the right hand and arm. In 1952 a right cervical rib was removed but he experienced no relief and since that time had had increasing weakness in the right arm and hand. He had loss of muscle bulk, es-



(a) (b) (c)

Fig. 3a.—Routine upper femoral injection vaguely showing arteriovenous shunt in calf. (b)—Percutaneous femoral catheter angiogram with tip of catheter in popliteal artery. Traumatic fistula between peroneal artery and vein well demonstrated (arrow). (c)—Postoperative femoral catheter angiogram showing disappearance of fistula and absence of immediate venous filling. The peroneal artery below the previous fistula site does not fill. The anterior and posterior tibial arteries are well shown throughout.

pecially of the right biceps, and weakness of the right brachial and radial pulse.

Percutaneous femoral catheterization was carried out and the tip of the catheter placed in the aortic arch close to the origin of the innominate artery. The resulting angiogram (Figs. 5a and 5b) showed complete occlusion of the right subclavian artery just distal to the origin of the thyrocervical trunk with collateral flow via the suprascapular and subscapular arteries into a narrow right axillary artery. Back-flow along the axillary artery showed the distal site of the block to be in the proximal portion of the axillary artery.

A right subclavian artery thrombosis was confirmed at operation, and grafting across the occluded segment was performed.

Detailed case material is not included in this paper as it is intended primarily to be a brief account of our experiences with catheter guide wire angiography.

COMPLICATIONS

If particular care is taken to use the lightest pressure in advancing the guide wire and catheter along the artery, no serious complications such as extraluminal injections, or unintended direct injections into branch arteries should be anticipated, provided a good flow back along the catheter is obtained immediately before injection, and a preliminary small test injection of 5 c.c. is given.

Nevertheless, Sutton[12] has recently emphasized that although he has seen no complication, such as large hematomas, among many hundreds of arterial catheterizations in normotensive patients, percutaneous arterial catheterization, particularly in hypertensive subjects, is not a procedure to be undertaken lightly or without considerable experience with arteriographic methods. He notes that in a series of 150 patients with hypertension who underwent bilateral selective renal angiography by the transfemoral route, he has had two cases where large hematomas at the puncture site have required surgical intervention. This prompts one to wonder what undetected hematomas may occur

Fig. 4.—Superior venocavogram. Almost complete occlusion by neoplasm (arrow).

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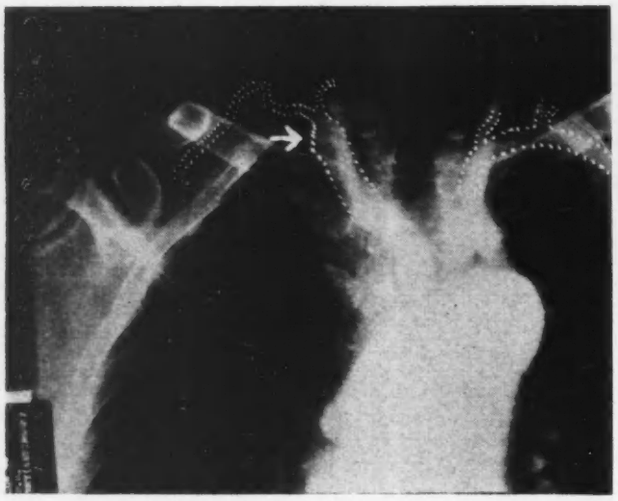

Fig. 5a.—Complete occlusion of right subclavian artery just distal to thyrocervical trunk (arrow). Compare normal left subclavian artery.

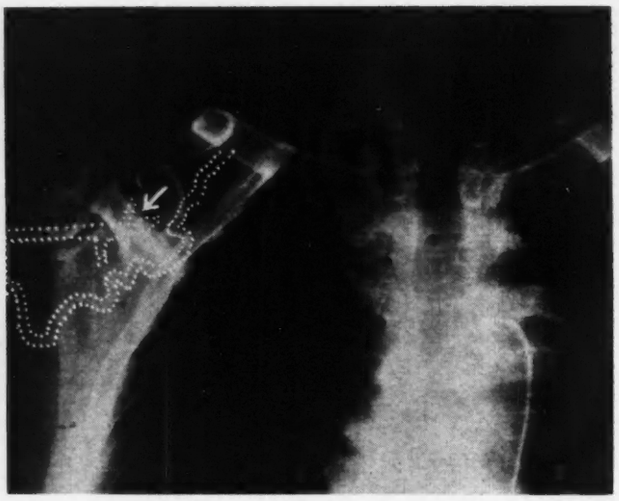

Fig. 5b.—Late film showing collateral arterial channels from thyrocervical region filling axillary artery retrogradely by way of the subscapular artery. The distal site of occlusion is thus shown (arrow). (Arteries are delineated by dotted lines.)

into the retroperitoneal tissues of hypertensive patients following translumbar aortography, where no pressure can be applied to the punctured vessel.

Recently two deaths have been reported in a series of 157 patients in whom this technique was used for cardiac catheterization,[8] but in one patient it was considered that there was no reason to attribute death to the particular technique, and in the other, extenuating circumstances were present.

One death and one major complication have recently been reported in the Canadian literature.[13]

We have experienced one major complication, but the relationship to the renal angiogram was not direct, and other factors may have played some part. The patient was a 63-year-old man with severe hypertension whose renal angiogram showed occlusion of the artery to the upper pole of the right kidney. Right nephrectomy resulted in a severe drop in blood pressure which was unstable but gradually settled to the 140/75 level. Three days after operation and 17 days after the angiogram he developed a thrombosis of his left femoral artery at the site of percutaneous puncture.

One or two of our patients developed small hematomas, but most had only minimal local discomfort at the puncture site.

COMMENT

Our own experiences with catheter guide wire angiography lead us to agree with those who consider it superior to translumbar aortography. In addition, it has much wider applications than the latter procedure.

We have not had the opportunity to use it in the investigation of arteriosclerotic aortic and aortoiliac abnormalities, and clearly one would be reluctant to carry out examinations for such conditions by the femoral route. In such circumstances the percutaneous brachial route may be used, although Wickbom and Bartley[14] and Lindbom[15] have shown that the brachial artery is sensitive to mechanical stimulation and readily goes into spasm followed by thrombosis. Particular care must therefore be used in employing this route, whether for aortography or any of the other forms of angiography for which it may be used. Further refinements in technique[9] may lessen the chances of this complication.

Apart from obviating the possible dangers of intramural or extramural aortic injection, or inadvertent direct injection into a branch artery, the ability to carry out the catheter-type examination with the patient in the supine position, instead of the prone one necessary for translumbar aortography, has great advantages in patient comfort and co-operation as well as in ease of radiographic positioning. Furthermore, a good concentration of dye can be easily obtained by manual injection, as compared with the hard manual injection or the mechanical pressure injection that is usually necessary for translumbar aortography.

Although the catheter guide wire technique offers virtually no advantages in the investigation of diffuse peripheral vascular disease of the limbs, it is of great value in the investigation of peripheral arteriovenous malformations. It enables adequate concentrations of dye to be obtained in these lesions, despite the very rapid blood flow which so adversely affects concentration if the injection is some distance from a shunt.

As already noted, our own use of the technique has been relatively limited, but the literature from other countries describing its uses and advantages in many anatomic regions indicates that there is virtually no part which cannot be successfully examined by the percutaneous puncture of a peripheral vessel.

One should nevertheless conclude on a note of caution in regard to undertaking the use of these angiographic techniques.

SUMMARY

Experiences with the percutaneous catheter spring-guide technique of angiography devised by Seldinger

are described. Examples of its uses in various anatomical regions (excluding angiocardiography) are given. Its advantages, particularly as compared with translumbar aortography, are discussed. Possible complications and ways to minimize them are indicated, and the views of others with wider experience are cited.

No angiographic technique, whether by indirect catheter or direct puncture, should be undertaken lightly.

I should like to express my thanks to those colleagues who have encouraged this work and have referred their patients for examination. I am also greatly indebted to those members of the nursing and x-ray technical staffs and to my secretary, all of whom have given so freely of their time and skill.

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FAILURE OF REGENERATION OF SMALL BOWEL MUCOSA FOLLOWING EPIDEMIC INFANTILE GASTROENTERITIS*

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INFANTILE gastroenteritis is a clinical syndrome characterized by diarrhea, vomiting and dehydration in which certain serological types of *E. coli* often can be isolated from the stools. Most infants recover after the acute stage, but a few become progressively emaciated despite treatment and die after an illness lasting several weeks. This paper is an account of the pathological changes found in the intestines of four such emaciated infants who died during the course of an epidemic of *E. coli* diarrhea.

MATERIAL

Autopsies were performed on four infants who had diarrhea and vomiting, associated with the presence of *E. coli* O 111 in their intestinal tracts. Three of these infants were treated in hospital for dehydration, and, after preliminary periods of starvation, were fed with increasing amounts of cows' milk but failed to gain weight and died. The fourth infant (98/58) had been in hospital with pneumonia and developed diarrhea and vomiting on returning home; after two weeks she became intensely dyspneic and died. All four infants failed to gain weight, and their weights at death were little more than they had been at birth (Table I).

TABLE I.—AGE, WEIGHT, AND FOOD INTAKE OF FOUR INFANTS WITH DIARRHEA AND VOMITING ASSOCIATED WITH *E. coli* O 111 INFECTION

Code number	*Birth weight g.**	*Weight at death g.**	*Age at death weeks*	*Length of illness weeks*	*Mean daily intake during terminal illness*	
					*calories**	*protein g.**
224/58	2500	5400	36	3	200	4
204/58	2800	3200	16	5	440	15
149/58	1600	2400	12	5	150	9
98/58	2700	3700	12	2	unknown (at home)	

*Weights and calories in this table are expressed to two significant figures only.

The most striking feature at autopsy was the external appearance of emaciation, which was so marked that starvation appeared to be a contributory cause of death (Fig. 1). In each infant there was loss of body fat and atrophy of the internal organs, but in one infant (224/58) the emaciation and weight loss were partly obscured by edema. In each infant the esophagus and stomach were normal, but pathological changes had occurred in the small and large intestines. These changes were generalized and consisted mainly of moderate to

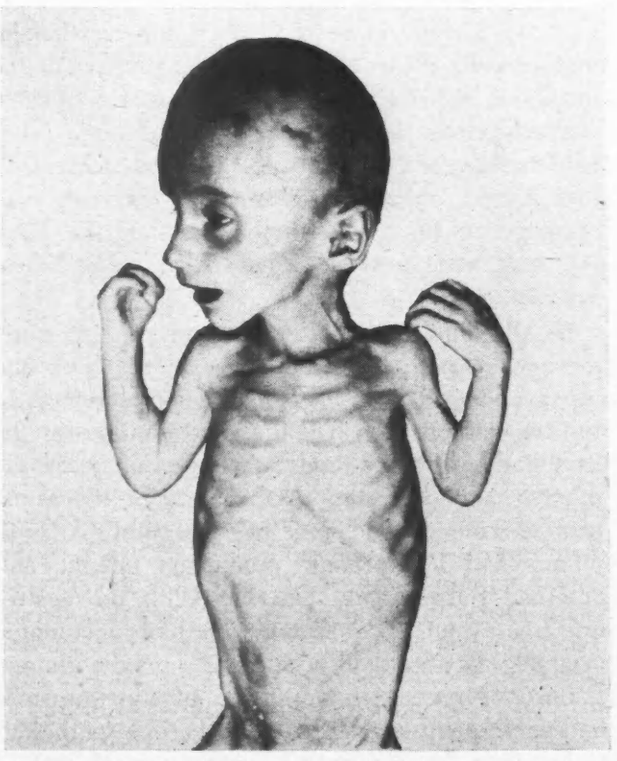

Fig. 1.—Photograph of an infant (204/58) taken at autopsy to illustrate the severe emaciation which may follow epidemic gastroenteritis.

*From the Department of Pathology, Dalhousie University and the Pathology Institute, Province of Nova Scotia, Halifax, N.S.

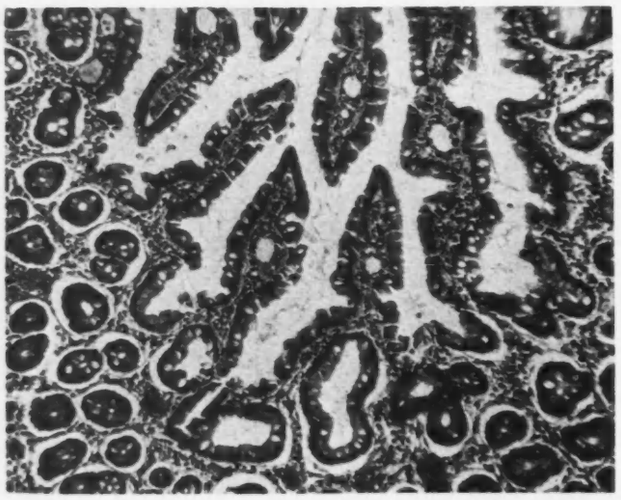

Fig. 2.—Photomicrograph of normal infant's intestinal mucosa with well-formed villi. Hematoxylin and eosin.

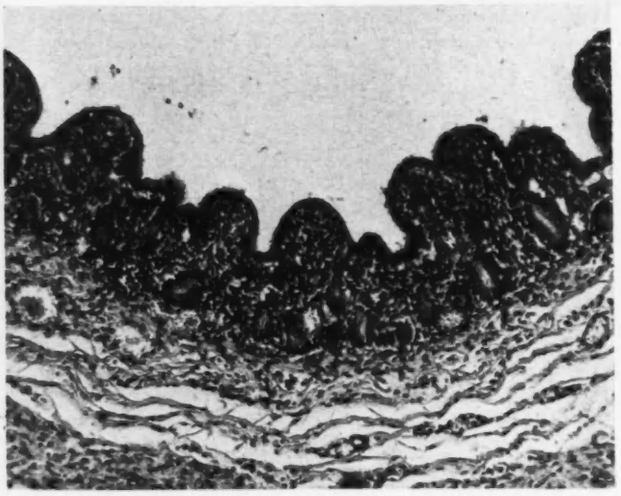

Fig. 3.—Photomicrograph of intestinal mucosa of an infant (98/58) with prolonged gastroenteritis. The mucosa is abnormally thin and its surface area is greatly reduced by lack of villi. Hematoxylin and eosin.

marked congestion of the mucosa, and slight but definite flattening of the mucosal folds. There were no gross localized ulcers, and dilatation of the bowel was either absent or minimal. Microscopically, the small bowel mucosa was extremely thin and was structurally simplified. The villi in the small intestine were either absent or only poorly formed, so that the total surface area available for digestion and absorption must have been considerably reduced. The smooth mucosal surface was covered with a layer of flattened epithelial cells, only a few of which contained mucin vacuoles (Figs. 2 and 3). Similar flattened cells lined the crypts of Lieberkühn and in these cells there were more mitotic figures than normal; some of the crypts were distended and appeared cystic. There was only a slight increase in the number of inflammatory cells present in the lamina propria of the intestinal mucosa; the submucosa was congested and edematous in two infants. In the large intestine there were similar but less marked changes. In one infant, microscopic areas of necrosis had occurred in the mucous membrane of the large intestine and in these areas there were fungal mycelia.

In addition to the alterations in the intestines there were pathological changes in the liver and lungs, and evidence of a hemorrhagic tendency. In the two infants who had the shortest illnesses the liver had undergone moderate fatty change; in the other two the liver was not fatty but contained excess hemosiderin and some bile "thrombi". All four infants had hemorrhagic pulmonary edema, and one had purpura and had bled into the gastrointestinal tract. The infant who had pneumonia originally (98/58) died because of a pneumothorax. Failure of regeneration of the intestinal mucosa and subsequent starvation were the only pathological causes for emaciation which were found at autopsy.

DISCUSSION

The pathological changes described above differ from those found in the acute stage of epidemic infantile gastroenteritis. In the acute stage, subcutaneous fat is still present and weight loss may be due to dehydration but not emaciation. The intestinal tract is often dilated, particularly when there has been potassium loss, the mucosal lining is ulcerated, and there is fatty change in the liver. By contrast, in infants who have died several weeks after the onset of diarrhea and vomiting, there is emaciation but not dehydration, the intestinal mucosa is simplified but not actively ulcerated, and fatty change in the liver is no longer a prominent feature. The presence of bile "thrombi" and excess hemosiderin in the livers of infants with prolonged gastroenteritis has been observed previously,[1] and a hemorrhagic tendency in such infants has been attributed to prothrombin deficiency.[2]

In infants who have died during the acute stage of epidemic gastroenteritis, microscopic changes in the intestinal mucosa tend to be obscured by autolysis. However, it is apparent that any damage present must be widespread and that localized ulcers are not a constant feature.[3, 4] Experiments on animals suggest that enteropathogenic *E. coli* may produce widespread superficial destruction of intestinal epithelium and loss of villi;[5] this might well occur in human infants and would be compatible with the cholera-like clinical features of infantile gastroenteritis. In infants who have died several weeks after the onset of diarrhea and vomiting, the reduction in depth of the intestinal mucosa and the lack of villi are best explained by failure of regeneration of the mucosa following widespread superficial destruction during the acute stage. Such failure of regeneration might result from malnutrition when tissue protein was being used for the release of energy and was not available for reparative purposes. The possibility that thinning of the mucosa is due to persistent active infection is not supported by the pathological

findings; inflammatory changes are minimal and ulceration is absent. In malnourished infants, if the intestinal mucosa fails to regenerate there will be continued impairment of digestion and absorption. This leads to further malnutrition, which cannot be corrected by oral feeding, and consequent starvation. In the infants described above this appears to have been the underlying mechanism of death.

Summary

A description has been given of the pathological changes found in four infants who died of starvation several weeks after the onset of *E. coli* enteritis. Failure of regeneration of the intestinal mucosa and severe general emaciation were outstanding features, and these have been contrasted with the changes found during the acute stage of the disease. The relation between malnutrition and failure of regeneration of the mucosa has been discussed.

One of the autopsies described above was performed by Dr. N. Kerenyi, who kindly allowed us to include his observations in this paper.

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TREATMENT OF ACNE WITH PROTHIPENDYL

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In any dermatological practice, one may count on seeing daily two or more patients suffering from acne vulgaris and, less commonly, from acne rosacea. Although the treatment of acne vulgaris is on the whole unsatisfactory, highly gratifying results both to patient and to physician are often obtained. Hormonal stimuli are a basic factor in the development of some vulgaris, but there is no practical method of attacking the etiology of the disease by influencing them. Treatment is therefore limited in many cases to local therapy, elimination of foods or drugs which aggravate inflammatory processes, combating secondary infection with antibiotics and vaccines, and use of ultraviolet light or sunlight. These are only a few of the measures employed. The passage of time is often very important and must be kept in mind in the assessment of any method of treatment.

Any new aid in treatment which will produce improvement in a sufficiently large percentage of cases is welcomed by most physicians. Such treatment is all the more eagerly received if it is simple, inexpensive and free from such encumbrances as repeated urinalyses, white blood cell counts, etc. The use of prothipendyl hydrochloride (Timovan), tried in 21 patients, appears to be of definite value in the treatment of this skin condition.

In the author's practice, many cases of acne in adolescents are seen to flare up in December and June when the patients are subject to the stress of writing school term examinations. In some adults, especially women, exacerbations of acne seem to stem from the stress of changing jobs, working overtime or trying to meet work quotas. Tranquillizers and sedatives have been used at times with frequent and undesirable side effects, particularly drowsiness and clouding of mental processes. When prothipendyl hydrochloride was submitted for clinical evaluation, it was hoped that its effectiveness would be matched by freedom from side effects.

Timovan or prothipendyl hydrochloride (4-dimethyl-amino-propyl-pyrido (3,2 beta) (1,4) benzothiazine hydrochloride-monohydrate) has the following structural formula:

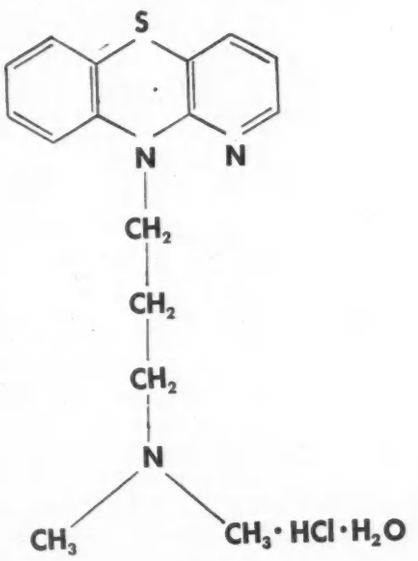

Fig. 1

Experiments on animals suggest that its action on the central nervous system is similar to that of chlorpromazine, while its effect on the autonomic nervous system is an inhibition or reversal of the action of adrenaline. It also weakly opposes the effect of acetylcholine. Certain animal experiments have shown that it has some antihistaminic property and that it produces an inhibition or a reversal of the action of serotonin. In man, the burning sensation and the degree of swelling and erythema inherent in histamine-induced wheals are reduced in intensity.

Electroencephalographic studies in humans revealed no sleep pattern differences and no ten-

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TABLE I

Case No.	Initials of patient	Age* and sex	Diagnosis	Duration of lesions before prothipendyl (Timovan*)	Medications used before administration of prothipendyl†	Prothipendyl dosage		Results after use of prothipendyl	Remarks
						mg.	times/day		
1	R.R.	16 M	Acne vulgaris, papulopustular	1	Sulfur-resorcin ointment, vitamin A, conjugated estrogens (system.)	25	3	Marked clearing of lesions in 10 days; improvement maintained.	Stuttering disappeared while patient was under treatment.
2	A.M.	16 F	Acne vulgaris, mild to moderate in intensity.	3	Sulfur-resorcin ointment, vitamin A, antibiotics, sulfonamides, estrogens, triamcinolone.	25 25 25	3 4 2	Marked clearing within 10 days.	Drowsiness on 75 mg. a day; no side effect on 50 mg.
3	W.A.S.	35 F	Acne rosacea of varying intensity	18	Sulfur-resorcin ointment.	25	3	Definite improvement in one month.	Flushing of the skin noticeably diminished.
4	W.S.	18 M	Acne vulgaris, cystic, moderately severe.	3	Vaccines, topical applications (unspecified).	25	3	Improvement in one month but not sustained.	
5	J.J.	18	Acne vulgaris, papulopustular.	5	Sulfur-resorcin ointment, conjugated estrogens (system.)	25	3	Skin cleared up within a month.	
6	L.D.	16 F	Acne vulgaris, papulopustular early cystic.	4	Acne diet, x-ray, vitamin A, tetracycline.	25	3	Progress of lesion stopped in 10 days; improvement thereafter.	
7	G.M.	24 F	Acne vulgaris, indolent papular.	4	Conjugated estrogens (system.), sulfur-resorcin ointment.	50	3	Complete clearing within 3 months.	More relaxed and comfortable.
8	N.K.	19 F	Acne vulgaris, small, papular.	3	Vitamin A.	25	3	Complete clearing within 3 weeks.	
9	M.H.	18 F	Acne vulgaris, papulopustular.	2	Hydroxyzine HCl.	25 25 25	4 3 4	Marked clearing within a month.	Complained of disturbing dreams on 100 mg.; dosage reduced to 75, dreams subsided; later raised again to 100 mg. without further side effects.
10	D.F.	15 M	Acne vulgaris, papulopustular at first, later severely cystic.	1	Tetracycline, methylprednisolone, 10% sulfur in a proprietary ointment.	25	3	Improvement noticed within a week, slowly progressive thereafter.	Feeling of well-being; diminished apprehension.
11	C.N.	34 F	Acne vulgaris, papulopustular.	4	Conjugated estrogens (topical and systemic), lotio alba, tetracycline.	25 25	3 4	No improvement.	
12	J.B.	13 F	Acne vulgaris, papulopustular low grade.	3	Lotio alba, vitamin A.	25	3	Definite improvement within 6 weeks.	
13	A.C.	23 F	Acne vulgaris, papulopustular.	8	Conjugated estrogens (system.), vitamin A, ultraviolet light.	25	3	Partial clearing rapidly achieved.	Produced best results of all medications used so far.
14	E.H.	26 F	Acne vulgaris, papulopustular mildly cystic.	6	Estrogens (systemic), vitamin A, tetracycline.	25 25 25	3 2 3	Definite and sustained improvement.	50 mg. insufficient to produce expected results and control exacerbations.
15	H.T.D.	23 F	Acne vulgaris, papulopustular, early cystic.	1½	Estrogens (systemic), unspecified topical medication.	25 25	3 4	Almost complete clearing in 5 weeks.	Tense patient became more placid.
16	A.J.	20 F	Acne vulgaris.	6	Thyroid globulin, estrogens (systemic), sulfur-resorcin lotion.	25	3	No improvement.	
17	D.C.	19	Acne vulgaris, cystic.	3½	Staph. vaccine, estrogens (systemic), sulfur-resorcin lotion.	25	3	No improvement.	
18	G.H.D.	36 F	Acne rosacea.	4	Diet, lotio alba.	25	3	Papules disappeared in a month; erythema eventually cleared up completely.	
19	C.Mc.	47 F	Acne rosacea, early rhinophyma.	17	Unspecified topical medication, vaccines, antibiotics, x-ray, 10% sulfur in proprietary ointment.‡	25	3	Improved within a month; almost normal skin in 10 months.	Felt calmer, slept better.
20	M.F.	28 F	Acne vulgaris.	14	Sulfur-resorcin lotion.	25	3	Cleared in 6 weeks.	
21	K.W.	16 F	Acne vulgaris, papular.	3	Diet, sulfur-resorcin ointment.	25	3	Almost clear in 2 months.	Second course as successful as first after reactivation.
22	G.H.	25 F	Acne rosacea.	1	Diet, sulfur-resorcin ointment.	25	3	Almost clear in 1 month.	
23	F.R.	19 F	Acne vulgaris, moderately severe.	5	Diet, sulfur-resorcin ointment, estrogens (systemic), ultraviolet light, perphenazine.	25	3	Almost complete clearing in 1 month.	
24	S.H.	16 F	Acne vulgaris, cystic.	2	Diet, vitamin A, ultraviolet light, sulfamethoxypyridazine, estrogens (systemic), 10% sulfur in proprietary ointment.‡	25	3	Some improvement within a month.	
25	R.W.	15 M	Acne vulgaris, papulopustular.	3	Diet, sulfur-resorcin ointment, conjugated estrogens (systemic).	25	3	Marked clearing within 2 weeks.	Facial tic disappeared while patient was receiving treatment.

*In years.
†Occasionally some of these were continued while patient was also receiving prothipendyl; most of the time they had procured no lasting benefit.
‡A proprietary ointment containing 10% benzoyl peroxide and 0.5% chlorhydroxyquinoline in petrolatum and lanolin.

dency to trigger latent epilepsy. Although itself devoid of narcotic property, the drug does intensify the effect of sedatives and analgesics. No evidence of toxicity or liver damage could be detected after prolonged use. In humans prothipendyl hydrochloride would therefore appear to lower spontaneous activity, temper intense emotional reactions and inhibit or depress central and peripheral sympathetic stimulating mechanisms and neurocirculatory reflexes.

At first, the drug was administered only to patients with acne vulgaris, but later it was also used in some with acne rosacea. In most cases it was given to patients who were already under treatment and failing to respond to the usual modalities. Sometimes these other forms of therapy were discontinued; at other times they were maintained with or without modification in administration. No attempt was made to control this experiment, as such a control would have been almost impossible to achieve. This report is a personal assessment of the clinical value of the drug and of the way it compares with accepted types of treatment in acne.

Case Reports

Data on the whole series of cases are presented in Table I. A few case reports were singled out at random so as to present the facts in greater detail.

Case 1.—R.B., a 16-year-old boy who stuttered, developed acne vulgaris in late 1956, as evidenced by large papulopustular lesions on the cheeks and chin. He was first seen in October 1957, when he was given the usual sulfur-resorcin creams and vitamin A in gradually reducing doses from 150,000 units to 50,000 units daily over a period of four months. Some improvement resulted, but the disease relapsed while he was on therapy. In July 1958 he was given conjugated estrogens (Premarin) 1.25 mg. daily for two months with some improvement. The same topical therapy thereafter produced no great change.

On March 14, 1959, he was given oral prothipendyl, 25 mg. thrice daily. Marked clearing of his complexion was noted in 10 days and the therapy was continued for three months, even though no new lesions developed. There were no side effects from treatment except that it was noted by his parents that the patient was less excitable and that his stuttering had disappeared. The patient was last seen in January 1960; his complexion was still quite clear.

Case 3.—W.A.S., a 35-year-old unmarried woman, had had various degrees of acne rosacea since the age of 17. When first seen on March 24, 1959, there was marked erythema of the nose and cheeks, and central portion of the forehead and chin, with scattered pustules throughout the involved areas.

The past history was uneventful apart from a cholecystectomy without sequelae in 1951. She had received no treatment for her skin condition apart from the usual sulfur-resorcin. When seen on May 20, after eight weeks of 25 mg. of prothipendyl thrice daily, there was a definite improvement in her acne rosacea. No new pustules had formed and the erythema was considerably reduced. The patient volunteered that she was not nearly so prone to flushing of the skin as she used to be.

This woman has been under much tension resulting from living with relatives. She has been followed up until early May 1960. On four or five occasions, during exacerbations, she requested the same therapy, with equally good results each time after a 7- to 10-day course. No untoward side effects have ever been noted.

Case 5.—J.J. is 18 years old. She developed a moderately severe papulopustular type of acne vulgaris in 1953, with early scarring, involving the cheeks, forehead and chin. This condition was usually worse before her menstrual periods and at times of excitement or stress. Her previous health had been excellent, and the only form of therapy she had received had been limited to the sulfur-resorcin medications.

She was first seen on December 29, 1958, and the only major change in therapy was the addition of conjugated estrogens 1.25 mg. daily, during intermenstrual periods. This brought about a 50% improvement. The patient attended an out-of-town university and she was next seen on March 31, 1959, when she was given prothipendyl 25 mg. thrice daily. This drug was well tolerated; she stated that while she was taking it her face had cleared up within a month. She continued the therapy for three months, and when seen on June 29 her complexion was completely clear.

Case 9.—This 18-year-old patient developed low-grade papulopustular acne about two years before her first visit on February 10, 1959. Her general health had been excellent, but she was an inveterate "picker". Thus the skin presented numerous crusts as a result of mechanical interference.

She was given hydroxyzine hydrochloride (Atarax) 10 mg. thrice daily for 40 days, without change. On March 21 she was given prothipendyl 25 mg. four times daily for one month. There was marked clearing of her skin during this period, and her "picking" habit almost disappeared. However, she complained of extremely disturbing dreams and after 11 days the dose was reduced to 25 mg. thrice daily and her upsetting dreams disappeared. The dose was increased to 25 mg. four times daily on April 10, because of a slight flare-up, without any untoward effects this time. The patient graduated from business college April 1 and immediately began working as a stenographer. Her skin did not reflect the increased tension associated with her new employment and when last seen July 2, 1959, it was still clear.

Case 14.—Miss E.H., aged 26, developed papulopustular acne of the face when about age 20, and within a year, she was afflicted with mild cystic acne in the same area. She would develop two to six cystic lesions every month or two, often during the week preceding her menstrual period, or otherwise when she was under emotional stress.

Her general health had been excellent; her acne had subsided in 1953 while she received estrogens intermenstrually for four months, but had recurred on cessation of treatment. In October 1958, when next seen, she was given 150,000 units of vitamin A daily for

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three months without any improvement. Papulopustular lesions appeared in the same areas in January 1959; she was given four courses of tetracycline 250 mg. four times daily for 5-6 days during the next three months, with temporary improvement.

From June 24, as the lesions were still recurring, she was given prothipendyl 25 mg. thrice daily until August 1. During this period a definite and sustained improvement was noted. The dose was then reduced to 25 mg. twice daily but this brought on a relapse. On August 18, the dose was increased to 25 mg. thrice daily and maintained until November. The larger dose produced definite improvement; when seen on December 1 her face was quite clear. It has since remained free from new lesions.

This patient presented a definite problem in therapy. There is no doubt that the tranquillizing effect exerted by prothipendyl prevented the development of new lesions.

Case 15.—H.T.D., a married woman of 23, was first seen on May 25, 1959. For the past 18 months she had suffered from a papulopustular type of acne vulgaris, involving the cheeks and chin. The lesions were becoming progressively more severe, and small cysts appeared in early 1959. New lesions usually came out in the premenstrual phase.

The patient's general health was excellent. Her personal history revealed that she had been rather spoiled throughout her formative years and, although married and the mother of two children, she was immature and unhappy in her marriage.

She received the usual topical medications in May 1959, and oral estrogen intermenstrually, without great benefit. On July 16 she was given prothipendyl 25 mg. thrice daily. When seen again five weeks later she was more placid and her face was almost clear. Therapy was maintained until September 24, when she noted a mild flare-up after a violent domestic quarrel. The dose was then raised to 25 mg. four times daily. She was next seen October 23, 1959, and her skin was then quite clear.

Case 25.—R.W.S., a 15-year-old boy, when first seen in August 1959 had been afflicted with acne vulgaris of the face and back for two years. It was of the moderately severe papulopustular type, which was producing a fair degree of scarring. His general health had been excellent.

He was first given the usual diet, resorcin-sulfur ointment and conjugated estrogens 1.25 mg. daily. When seen in early October there was a remarkable degree of clearing and the estrogens were reduced to 0.625 mg. daily for one month. There was further improvement in the course of the next month. He continued to adhere to the diet and to use the same ointment, but a flare-up occurred in December while writing examinations. Prothipendyl 25 mg. thrice daily was prescribed on January 16, 1960, and resulted in marked clearing of the lesions within two weeks.

He was a tense adolescent and the parents noted that a facial tic, present for two years, had disappeared. The drug was continued until late June 1960, and his face has remained clear.

Discussion

Prothipendyl hydrochloride has been used in 21 cases of acne vulgaris and four cases of acne rosacea. Marked improvement of the complexion followed its use. In all cases it was completely free of side effects, apart from transient drowsiness during the first two days of therapy in two patients, but this disappeared on continued use. In all instances there was no significant change in pulse and blood pressure or in urine findings.

In 17 of the 21 cases of acne vulgaris, marked clearing was noted within 30 days. In this group of 17 patients, the lesions in 13 had failed to respond to previous therapy or to remain under control for any prolonged interval. This series is too small to draw any definite conclusions, but the rapid improvement in 80% of cases and the freedom from side effects make prothipendyl an excellent drug in the treatment of acne, especially in patients who show exacerbations while under tension.

The parents of several adolescents afflicted with acne vulgaris noted that their children were less excitable, and in two instances reported the disappearance of facial tic and stuttering. It would therefore appear that the drug has a mild tranquillizing action.

In most cases of acne vulgaris, exacerbations were observed while the patients were under nervous tension, as for example when writing examinations. Such exacerbations failed to take place when the patients were receiving prothipendyl. In most instances there was a marked decrease in the oiliness of their skin. In the four cases of acne rosacea reported here, a considerable reduction in the degree of erythema was noted within 30 days.

Summary

Prothipendyl (Timovan) was given to 21 patients with acne vulgaris; remarkable clearing was observed in 17. Four patients with acne rosacea responded well to the same treatment. There were almost no side effects and the drug was well tolerated. Prothipendyl would appear to be an excellent form of treatment for patients whose acne sustains an exacerbation when they are subjected to emotional stress.

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SPECIAL ARTICLE

SOME APPLICATIONS OF STATISTICS TO MEDICAL RESEARCH*

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PART I OF FOUR PARTS

MEDICAL LITERATURE abounds with differences of opinion and these controversies tend to persist for years. Sometimes erroneous statements based on unwarranted conclusions from a few uncontrolled experiments are made which may not be refuted for years. There is a growing respect in medical circles for statistical methods and a realization that without adequate analysis conclusions are often merely opinions. However, it must be emphasized that statistical analysis of data cannot prove anything in an absolute fashion but only the likelihood of the results obtained being due to chance.

There is nothing mysterious about statistics; the theory is logical and the arithmetic is simple. Statistical analysis of data is not difficult and without analysis many reports in scientific journals are incomplete, for it is essential that real differences be separated from those due to chance. The following is an example. A certain disease when untreated is known to have a mortality rate of 50%. A new drug is developed for the treatment of this disease and administered to 6 patients of whom 1 dies and 5 recover for a mortality rate of 16.7%. On the basis of these results one might be led to believe that this drug has had a profoundly beneficial effect on the outcome of the disease. However, if subjected to analysis it will be found that this ratio (1 dies, 5 recover) would be expected to occur in untreated cases due to chance alone in about 9.4% of all 6-patient series. In fact, on the basis of this single test it is quite possible that the drug has had no effect whatsoever on the outcome of the disease process.

In this and subsequent articles some of the applications of statistical methods to medical research will be discussed so that with the aid of a good text[1] anyone engaged in medical research will be able to analyze critically his own data and assess the quality of work done by his colleagues. The material will be covered in the following fashion:

(1) Functions of statistics; methods of statistics; sampling; normal distribution; binomial theorem; mean, mode, median; variance; standard deviation.
(2) "*t*" test.
(3) Chi square.
(4) Linear regression and simple correlation.

FUNCTIONS OF STATISTICS

The functions of statistics are threefold:

(1) *To reduce the data.* This is done by compiling charts, tables, graphs, histograms (bar graphs), frequency polygons (continuous line graphs), etc., in an attempt to determine a trend or an average or some value characteristic of the whole.

(2) *To provide methods of applying tests of significance.* Tests of significance are used to separate real differences from those due to chance. For biological data the level of significance is arbitrarily set at 5% (p = probability = 0.05). In the above example if the mortality rate of the patients treated with the drug was lowered sufficiently such that the new value would be expected to occur due to chance alone in less than 5% of cases, the results are said to be significant. There would be a 95% probability that the new mortality rate was due to a change in therapy and only a 5% probability that it was due to chance. For a value to be highly significant the 1% level is arbitrarily chosen; i.e. $p = 0.01$. Thus there would be a 1% probability that the difference is due to chance and a 99% probability that there is a real difference between the two mortality rates. The level of significance could be set at 10%, 25%, or even 50%. However, then one would be much more likely to call a value significant when it was really due to sampling variation. On the other hand, the level of significance could be set at 0.1% ($p = 0.001$). This would have the disadvantage that real differences might be overlooked and be ascribed as being due to sampling variation. To be certain that a potentially toxic drug was safe for human use the level of significance might be set at 0.01% ($p = 0.0001$). This means that there would be less than 1 chance in 10,000 that any observed deleterious effects were due to the drug and not some other variable.

(3) *To provide a sound basis for experimental design.* In many instances a great deal more information could have been obtained with the same amount of work if the researcher had had a knowledge of statistical methods, and so planned his experiment. A good deal of thought must go into the design of an experiment because it may mean the difference between sound, scientific research and worthless data which yield little or no information.

METHODS OF STATISTICS

The methods of statistics are of two general types:

(1) Descriptive or large sample methods in which group characteristics are measured for the purpose of obtaining an accurate description of the group.

(2) Inferential or small sample methods. The characteristics of a small sample are measured and those of the population are inferred from the small sample. Biometry is the analysis and interpretation of biological data by small sample methods.

There are two types of data: enumeration data (quantitative or discrete data) and mensuration data

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*This work was done under the direction of Dr. R. C. Harrison, Professor of Surgery, University of Alberta.
†Surgical Fellow, University of Alberta Hospital; Graduate Student in Surgery, University of Alberta.

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Height In.	Frequency
62	2
63	3
64	5
65	8
66	10
67	13
68	18
69	15
70	9
71	6
72	5
73	3
74	2
75	1

Mean Height—68.0 inches

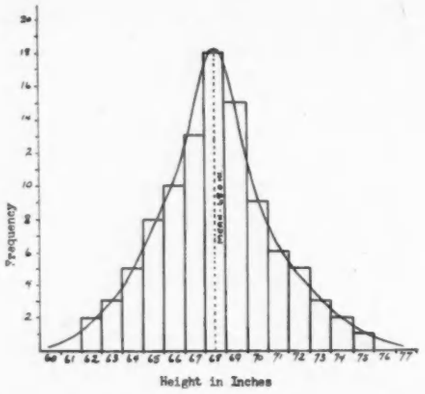

Fig. 1.—Frequency distribution of the height measurements of 100 mature white males.

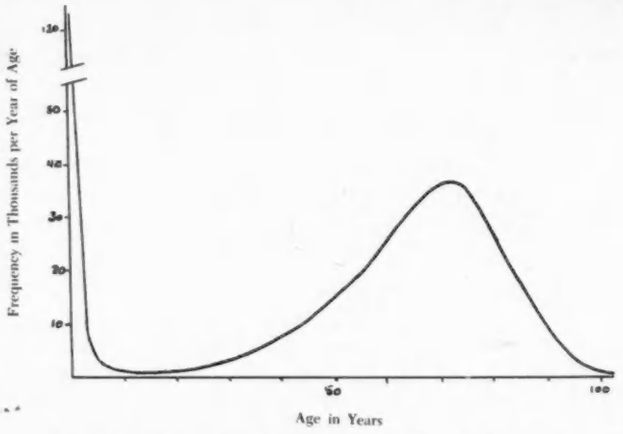

Fig. 2.—Frequency distribution of deaths by age.

(measurement or continuous data). Enumeration data always result in a particular set of values such as yes or no, death or recovery, etc. Mensuration data are records of measurements such as height or weight or blood pressure. The tests of significance for mensuration data and enumeration data are different, although the principles of statistical reasoning are the same for both.

SAMPLING

Since the statistician is often dealing with inferential methods, it is important that the characteristics of the small sample be a true indication of the characteristics of the population about which he may make generalized conclusions. For the sample to be representative of the population it must be obtained in such a way that no bias enters into its selection. For greatest likelihood of this being the case every individual in the population must have the same chance of being selected for the sample. There are many methods of sampling, and the choice of a particular method is up to the discretion of the researcher. An example of bias entering into the selection of the small group is shown in the following. We wish to study the natural history of measles and decide to examine all the cases of measles admitted to the communicable diseases ward of a large general hospital, over the period January 1960 to July 1960. Obviously there is at least one thing wrong with this study. We are studying a very select group: i.e. only those cases of measles that have been admitted to hospital. The vast majority of patients with measles recover at home and are never admitted to hospital. Thus those who are in hospital are admitted for some other reason such as the complications of measles—pneumonia, otitis media, encephalitis, etc., and the characteristics of this group will be very different from the whole population of people ill with measles. The criterion that every patient with measles has an equal chance of being selected for the small group study would obviously not be fulfilled.

NORMAL DISTRIBUTION

The primary purpose of statistics, the reduction of data to a single measurement or value that is descriptive of the population, is dependent upon the premise that natural populations tend to follow certain mathematical models, one of which is the normal distribution. The normal distribution is a frequency distribution in which there are many values clustered about the mean with progressively fewer values for greater distances from the mean. The normal distribution curve is also called the normal probability curve, for it not only indicates the distribution of the variates but also the probability of selecting a variate of a specified size from the distribution. Those variates furthest from the mean, i.e. in either tail of the distribution curve, have the largest deviations but the smallest probability of occurring. The much simpler binomial distribution approximates the normal distribution, particularly as the number of observations increases. Many statistical determinations are based on the normal distribution and researchers may go wrong in assuming that their data are normally distributed. For instance, one statistic that closely follows the theoretical normal distribution is the height of mature white males (Fig. 1). Something that does not follow the normal distribution is age at death (Fig. 2). The interpretation of data that are not normally distributed is often difficult.

BINOMIAL DISTRIBUTION

The formula for the binomial distribution is $(p + q)^n$, where "p" represents the probability of an event occurring and "q", (or $1 - p$), the probability of the event not occurring. "n" is equal to the number of observations. This results in a step-like distribution (Fig. 3), and if "p" and "q" are equal there is a symmetrical distribution about the mean. As "n" is increased the curve becomes smoother and approaches the normal distribution. The normal distribution has an infinite range above and below the mean.

Example of Binomial Distribution

Suppose we are tossing a coin. There are two possibilities: a head or a tail.

The probability that a head or a tail will occur on any particular toss is 0.5 in each case. If we have

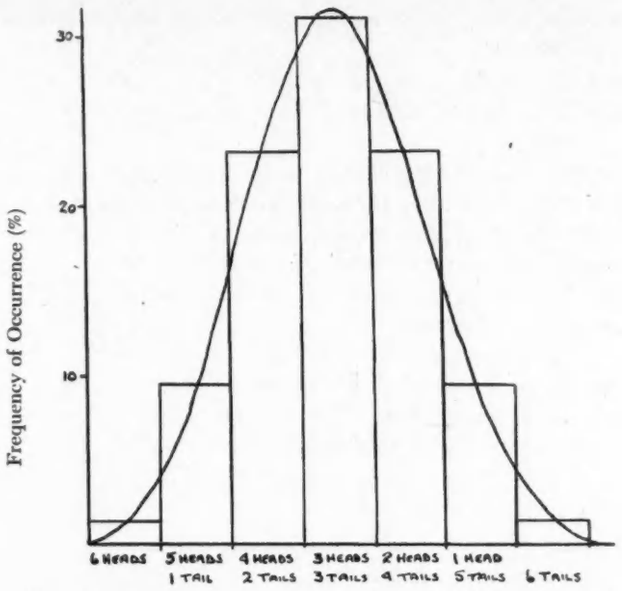

Fig. 3. — Frequency graph of binomial distribution of $(0.5 + 0.5)^6$.

two coins and toss them both at the same time, there are three possibilities:

(1) Two heads.
(2) One head, one tail.
(3) Two tails.

For a single throw of two coins the binomial distribution is applied as follows:

$$p = 0.5; \qquad q = 0.5; \qquad n = 2.$$
$$(p + q)^2 = p^2 + 2pq + q^2 = (0.5)^2 + 2(0.5 \times 0.5) + (0.5)^2$$
p^2 = probability of 2 heads = 0.25.
$2pq$ = probability of 1 head, 1 tail = 0.50.
q^2 = probability of 2 tails = 0.25.

Therefore, from a number of throws of two coins one would expect 50% of the throws to yield one head and one tail, 25% two heads and 25% two tails. Now suppose there are 6 coins and they are all tossed at once. There are now 7 possibilities:

(1) 6 heads
(2) 5 heads, 1 tail
(3) 4 heads, 2 tails
(4) 3 heads, 3 tails
(5) 2 heads, 4 tails
(6) 1 head, 5 tails
(7) 6 tails.

Expansion of the binomial distribution results in the following:

$$(p + q)^6 = p^6 + 6p^5q + 15p^4q^2 + 20p^3q^3 + 15p^2q^4 + 6pq^5 + q^6.$$

Substituting in the above equation for "p" and "q" results in the following:

$$(0.5)^6+6(0.5)^5(0.5)+15(0.5)^4(0.5)^2+20(0.5)^3(0.5)^3 +15(0.5)^2(0.5)^4+6(0.5)(0.5)^5+(0.5)^6$$

Expected Frequency of Occurrence

p^6	1.56%	6 heads
$6p^5q$	9.38%	5 heads, 1 tail
$15p^4q^2$	23.44%	4 heads, 2 tails
$20p^3q^3$	31.25%	3 heads, 3 tails
$15p^2q^4$	23.44%	2 heads, 4 tails
$6pq^5$	9.38%	1 head, 5 tails
q^6	1.56%	6 tails

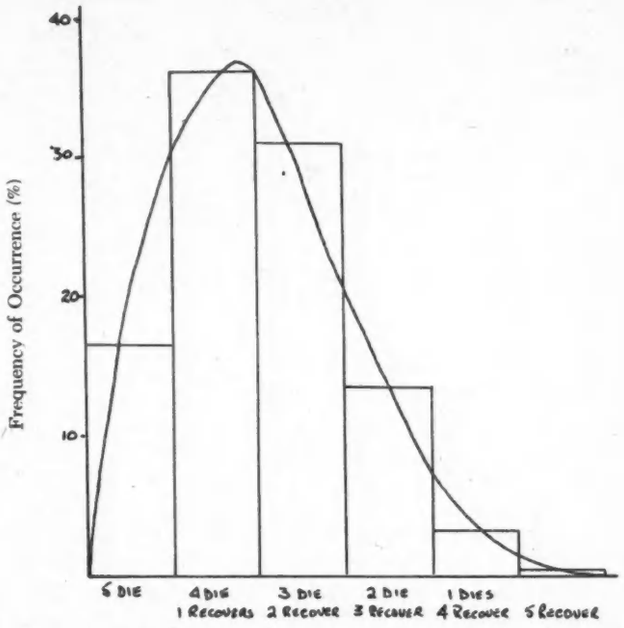

Fig. 4. — Frequency graph of binomial distribution of $(0.7 + 0.3)^5$.

Fig. 3 is a graph of these results.

"p" and "q" need not be equal. Suppose a disease has a mortality rate of 70%. Of five patients with this disease the possibilities are:

(1) five die
(2) four die, one recovers
(3) three die, two recover
(4) two die, three recover
(5) one dies, four recover
(6) five recover.

Substitution in the binomial distribution will give the frequencies with which these values would occur if the sample were representative of the population.

$$p = 0.70; \qquad q = 0.30; \qquad n = 5$$
$$(p + q)^5 = p^5 + 5p^4q + 10p^3q^2 + 10p^2q^3 + 5pq^4 + q^5$$

Substitution results in the following:

$$(0.7)^5 + 5(0.7)^4(0.3) + 10(0.7)^3(0.3)^2 + 10(0.7)^2(0.3)^3 + 5(0.7)(0.3)^4 + (0.3)^5$$

Expected Frequency of Occurrence

p^5	16.81%	5 die
$5p^4q$	36.02%	4 die, 1 recovers
$10p^3q^2$	30.87%	3 die, 2 recover
$10p^2q^3$	13.23%	2 die, 3 recover
$5pq^4$	2.83%	1 dies, 4 recover
q^5	0.24%	5 recover

Fig. 4 is a graphic representation of this distribution.

MEAN, MODE AND MEDIAN

When a series of observations has been recorded, it may be desirable to select a single value which is characteristic of the whole. One of these statistics is the arithmetic mean. It is the sum of the variables divided by the number of variables: $\frac{(\Sigma X)}{n}$.* One disadvantage of the mean is that depending upon the

*The Greek letter Σ (sigma) is commonly used to mean "the sum of".

TABLE I.

No. of sultans	*No. of wives per sultan*
1	1
3	2
4	3
8	4 Mode
6	5
7	6 Median
6	7
4	8
3	9
2	10
1	11
45	

Total number of wives = 255

$$\text{Mean} = \frac{255}{45} = 5.67$$

data it may be unrealistic. For example, in a survey of harems it was found that the mean number of wives per harem was 5.67 and the mean number of children per harem was 64.87. Now 0.67 of a wife and 0.87 of a child are difficult concepts to grasp and obviously some other statistic should be used (Table I).

The median in a frequency distribution is the value on either side of which lie an equal number of variates. In Table I the median is six wives per harem; five variates lie above and five below this value. An advantage of the median is that it is not influenced by the numerical magnitude of the individual deviations from the median. It is a good measure of the central tendency in a sample when it is desirable to suppress the influence of variates at extreme distances from the median.

The mode is the class with the greatest frequency provided the class interval is equal. It is also called the modal or most fashionable class. In Table I the mode is four wives per harem since more sultans had four wives than any other number.

Neither the mean, mode nor median reveals much about a population. It indicates nothing about the range of the values or the dispersion of individuals about the average. In the condensation of data the range is often used, but, although it indicates the highest and lowest values obtained, it tells nothing about the frequencies with which these values (and other values in between) have occurred. A possibility is to calculate the sum of the deviations from the mean, but those values above the mean will cancel those values below and the sum of the deviations from the mean will be equal to zero.

VARIANCE

A better measure of the dispersion is the sums of the squares of the deviations from the mean divided by the number of variates. This is the variance. It is not directly related to normal probability, and as a measure of variability it is difficult to interpret, because the original unit of measurement is squared. This is avoided by taking the square root of the variance. This is the standard deviation or standard error and is the most widely used measure of dispersion. The formula for calculating the standard deviation is

$$\text{S.D.} = \frac{\Sigma(X - \bar{x})^2}{n}$$

where X is the variate, $\bar{x}$ is the mean and n is the number of variates. Its units are those of the measurement involved, i.e. inches, pounds, etc. If there is a small number of variates, say less than 30, $n - 1$ in the denominator gives a better estimate of the standard deviation.

There are several methods of calculating the standard deviation. Two of them are as follows:

(1) Direct method. First calculate the arithmetic mean and proceed as shown in the example.

$$\bar{x} = \frac{\Sigma X}{n} = \frac{32}{8} = 4$$

X	$X - \bar{x}$	$(X - \bar{x})^2$
1	−3	9
1	−3	9
3	−1	1
4	0	0
4	0	0
5	+1	1
6	+2	4
8	+4	16
32		40

$$\text{Variance} = \frac{\Sigma(X - \bar{x})^2}{n - 1} = \frac{40}{7} = 5.7$$

$$\text{S.D.} = \sqrt{\frac{\Sigma(X - \bar{x})^2}{n - 1}} = \sqrt{5.7} = 2.4$$

(2) Variable Squared Method.

The development of the modern calculating machine has reduced the work of simultaneously squaring and adding of numbers to a simple mechanical task but has not facilitated subtraction to the same degree. Therefore to avoid subtraction it is often far easier to square and add relatively large numbers. The variable squared method employs the following relationship:

$$\text{sums of squares}^* = \Sigma X^2 - \frac{(\Sigma X)^2}{n}.$$

This is derived as shown in the series of equations at the top of page 435.

There are several other methods for calculating the sums of squares.[2]

The standard deviation is related to the normal distribution in the following way. The mean plus or minus one standard deviation includes 68% of the population, and if an individual were selected at random from the population there would be a 68% probability that its value would lie between these limits. The range, mean ±2 S.D., includes 95% of the population and mean ±3 S.D. includes 99% of the population.

*Shortened from sums of squares of deviations from the mean.

$$\Sigma(X - \bar{x})^2 = \Sigma(X^2 - 2X\bar{x} + \bar{x}^2) = \Sigma X^2 - 2\Sigma X\bar{x} + \Sigma\bar{x}^2$$

$$= \Sigma X^2 - 2\Sigma X\left(\frac{\Sigma X}{n}\right) + \Sigma\left(\frac{\Sigma X}{n}\right)\left(\frac{\Sigma X}{n}\right) \qquad \left(\text{since } \bar{x} = \frac{\Sigma X}{n}\right)$$

$$= \Sigma X^2 - 2\Sigma X\left(\frac{\Sigma X}{n}\right) + \Sigma X\left(\frac{\Sigma X}{n}\right) \qquad \left(\text{since } \Sigma\left(\frac{\Sigma X}{n}\right) = \Sigma X\right)$$

$$= \Sigma X^2 - 2\frac{(\Sigma X)^2}{n} + \frac{(\Sigma X)^2}{n}$$

$$= \Sigma X^2 - \frac{(\Sigma X)^2}{n}$$

X	X^2
1	1
1	1
3	9
4	16
4	16
5	25
6	36
8	64
32	168

$$\Sigma X = 32$$

$$\frac{(\Sigma X)^2}{n} = \frac{32 \times 32}{8}$$

$$\text{Sums of squares} = \Sigma X^2 - \frac{(\Sigma X)^2}{n}$$

$$= 168 - \frac{32 \times 32}{8} = 40$$

$$\text{Variance} = \frac{40}{7} = 5.7$$

$$\text{S.D.} = \sqrt{5.7} = 2.4$$

A large standard deviation in proportion to the mean indicates that the data are very variable and their validity may be open to question. The large variability may be due to one or both of the following:

(1) The biological material is very variable, in which case the criteria for selection of the small sample group may have to be applied within closer limits.

(2) The measuring device lacks precision. For example, the hemoglobin content of a sample of blood is measured 30 times each by two different methods (A and B). The values for method A are: 14.0 ± 0.9 g. % and for method B: 14.6 ± 0.4 g. %. It is obvious (since the standard deviation is smaller in proportion to the mean) that the variability of method B is less than that of method A. Method B is therefore the more precise method.

SUMMARY

The importance of analysis of data in medical research is emphasized. Some functions and methods of statistics are described. Basic statistical concepts are discussed, and methods of calculation are demonstrated.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

THE ONTARIO MEDICAL COUNCIL

The Ontario Medical Council is at present under a cloud; and all thoughtful observers are agreed that the time has come for a complete change in methods, and a careful scrutiny of the objects for which the council exists. When the council was instituted, provincial medical standards were low. Proprietary schools were to the fore, the universities were, in the true sense, without medical faculties, and the new arrangement came as a solution of a great difficulty. Yet it was full of danger, as "homoeopaths" and "eclectics" had to be recognized; and they secured representation out of proportion to their rights, even then, but extremely so at the present time. The council obtained absolute control of the situation, even such an institution as the University of Toronto giving up its claim to grant degrees carrying the right to practice. Wise men of the early days foresaw the inevitable, and a well-known president of the Canadian Medical Association, as far back as 1878, spoke pessimistically of the situation.

Possibly the situation was not quite so humiliating as it was believed to be; but, even in those days, it was frankly admitted that many members of the medical council could be classified as "politicians" by whom personal advancement was more thought of than the interests of the public, or of the profession itself. The council was always interested in medical education, and, while proprietary schools existed, went to great trouble to uphold its standards, which were, on the whole, fairly good, although by no means so heaven-inspired as they insisted. The schools were regarded with suspicion, sometimes with hostility, and elaborate precautions were taken to extract the stings from the professors' tails, as shown by the unique arrangement of examiners. If Professor A taught chemistry he might easily qualify as examiner in surgical anatomy, but could not examine in his own subject; homoeopaths were called on to examine in "regular" subjects.—Excerpt from editorial, *Canadian Medical Association Journal*, 1: 151, February 1911.

Canad. M. A. J.
Feb. 25, 1961, vol. 84

CASE REPORTS

ACUTE DIVERTICULITIS OF THE CECUM*

GENDRON MARCOUX, F.R.C.S.[C], F.A.C.S., CHARLES PLAMONDON, F.R.C.P.[C] and GUY BERTRAND, M.D., *Quebec City, Que.*

MRS. L.E., a 38-year-old woman, was admitted to the hospital on November 5, 1957, complaining of pain in the right lower quadrant, which had started approximately 48 hours before her admission and had increased in intensity, forcing the patient to bend over. The patient stated that her abdomen had been slightly distended for the previous few days. She noticed constipation for the previous three days, without nausea or vomiting. The patient reported that during the past year she had had several bouts of pain in her abdomen associated with nausea. There was a weight loss of 10 lb. because the patient refrained from eating for fear of pain. Otherwise there was nothing of further relevance in her history.

The patient, a well-nourished woman, appeared acutely ill. The abdomen was slightly distended and there was marked tenderness with muscular rigidity in the right iliac fossa. A mass was thought to be palpable over McBurney's point. Her temperature was 99.2° F. and her pulse rate was 80 per minute. The leukocyte count was 9000 with a normal differential count. A diagnosis of tumour of the cecum or of the ascending colon was made, and the patient was prepared for surgery with the usual preoperative schedule of neomycin.

At operation, there was a mass about 6 cm. in diameter on the medial aspect of the ascending colon just above the ileocecal valve. There was marked edema around the valve, and several enlarged lymph nodes could be seen in the mesentery.

A frozen section was made from the mass, and the report stated that this showed a chronic inflammation with the possibility of diverticulitis. A resection which included 12 cm. of the terminal ileum and 6 cm. of the ascending colon was performed. The distal ileum was then anastomosed in end-to-end fashion to the ascending colon; after obliterating the right peritoneal gutter and reconstructing the mesentery, the abdomen was closed in the usual manner with drainage.

The postoperative course was uneventful and the patient was sent home on the eighth postoperative day. A year after the operation the patient was in good general condition. She has had no further bowel complaints.

Pathological Findings

Gross examination.—The specimen consisted of the cecum, a small portion of the ascending colon and 12 cm. of the ileum. On the anterior aspect of the cecum, in proximity to the ileo-cecal valve, there was a superficial mass measuring 6 x 4.5 x 2.5 cm. in diameter, very firm, reddish, slightly lobulated and with a wide implantation. The mass had been opened surgically, revealing a cavity resembling a diverticulum, 15 mm. in depth, which communicated with the cecal lumen by an opening 15 mm. wide. The interior aspect was reddish with yellow streaks. In the adjacent mesentery there were several hard reddish lymph nodes.

Microscopic examination.—The aforementioned cavity was partly covered with mucus-secreting epithelium of colonic type. The wall was deprived of its muscular coats except for the muscularis mucosae. The mucosa was partially ulcerated and replaced by a thick fibrinopurulent layer. The surrounding tissue was infiltrated by edema with some hemorrhagic and fibrinous foci. The lymph nodes showed an acute reactive adenitis. The appendix was normal. The pathological diagnosis was acute ulceropurulent diverticulitis of the cecum with regional lymphadenitis.

COMMENT

This case is presented because of the rare incidence of this disorder.[1, 2] Up to 1955[3] only 166 cases had been reported in the literature. Colonic diverticula are almost invariably false; on the other hand, diverticula of the cecal type are nearly always true diverticula,[4] since their walls include all the layers of the gastrointestinal tract.

The etiology of cecal diverticula seems quite different from that for those in the remainder of the colon. The cecal diverticulum is usually solitary and occurs in a lower age group.

Several authors favour the embryological theory of origin of these lesions because of their similarity to enterogenous cysts or reduplication of the bowel.

A definite preoperative diagnosis of a cecal diverticulum is almost impossible to establish; it may be suspected if an appendectomy has previously been performed. The symptoms and diagnosis of cecal diverticulitis are identical with those of acute appendicitis or one of its immediate complications. The lesion is usually recognized at the time of operation, but even then it is sometimes difficult to exclude carcinoma,[5] and a frozen section for immediate microscopic examination is desirable.

Diverticulectomy, resection of the cecum and ascending colon, inversion of the diverticulum, hemicolectomy and drainage are the procedures that may be performed in varied circumstances.

A small, early, acutely inflamed diverticulum may be inverted with a purse-string suture. A larger diverticulum will require excision;[6, 7] if the inflammatory process is extensive, resection of the involved bowel may be required.

SUMMARY

A case of acute diverticulitis of the cecum is presented. Acute cecal diverticulitis is an uncommon entity. The diagnosis is usually made at the time of operation. The lesion is ordinarily of the pulsion type and con-

*From the Services of Surgery and Medicine, l'Hôpital de l'Enfant-Jésus, Quebec City.

genital. Unnecessary surgery is often performed because of an incorrect diagnosis of a malignant lesion. The operation of choice is local excision.

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INOPERABLE CARCINOMA OF THE CERVIX: PRELIMINARY REPORT OF A CASE AND A NEW APPROACH TO TREATMENT

W. N. KEMP, M.D., *Vancouver, B.C.*

THE FOLLOWING case report is presented to illustrate the efficacy of treatment of late invasive carcinoma of the cervix uteri by a combination of chemotherapy, radiation therapy and radical surgery.

On January 27, 1960, Mrs. L., a 40-year-old woman, para ii, was found to have a sloughing, fungating mass protruding from the uterine cervix. On pelvic examination it was noted that her uterus was firmly fixed to the pelvic wall. Biopsy from the cervical mass revealed areas of extensive degeneration and disintegration scattered among the remaining endocervical glands and connective tissue, deep to which was a large sheet of extremely poorly differentiated cells with numerous bizarre nuclei and multiple mitotic figures, with very little or no background stroma. A diagnosis of advanced (Stage III) invasive, anaplastic, squamous cell carcinoma of the cervix was made.

The following regimen of treatment comprising a combination of "saturation" androgen therapy, radiotherapy and antitumour chemotherapy was immediately commenced. Testosterone propionate* was administered intramuscularly in daily doses of 100 mg. When intramuscular injection was undesirable or impractical, a comparable androgenic effect was obtained by the oral administration of 50 mg. of fluoxymesterone† daily. Radiation therapy consisted of a single intrauterine radium implantation followed by a four-week course of cobalt beam gamma ray therapy. Thereafter cyclophosphamide‡ was administered intravenously in doses of 200 mg. every 12 hours for 12 days, to a total of 4.8 g.

Over the ensuing weeks the pelvic tumour appeared to undergo remarkable regression and on June 20, 1960, a modified Wertheim hysterectomy was performed without difficulty. At operation no definite evidence of residual carcinoma was noted in the pelvis or elsewhere. Sections of the uterus, cervix and regional lymph nodes likewise failed to reveal any microscopic remnants of active carcinoma.

During the administration of radiation therapy the patient experienced no appreciable irradiation sickness, nor was any anorexia or nausea noted during her intensive course of treatment with cyclophosphamide. During the period of administration of the latter drug her daily leukocyte counts at no time fell below 7000 per c.mm.

The only untoward effects observed were the manifestations of virilism due to her androgen "saturation" therapy and alopecia associated with the massive dose of cyclophosphamide. The masculinizing effects of the androgen consisted of acne, hirsutism and deepening of the voice. These did not constitute a serious handicap and were more than offset by a return of the patient's sense of well-being and gain in weight associated with this therapeutic regimen. The alopecia responded most satisfactorily to a two-month course of full doses of triamcinolone acetonide.

COMMENT

It is suggested that a combination of "saturation" androgen therapy and antitumour chemotherapy with cyclophosphamide, followed by adequate radiotherapy, may be capable of causing sufficient tumour regression in certain cases of primary inoperable carcinoma of the cervix to permit subsequent surgical extirpation of the primary malignancy. Simultaneously the carcinocidal effect of the circulating antitumour chemotherapeutic agent may be capable of controlling the development of metastatic lesions.

2414 Main Street,
Vancouver 10, B.C.

*The testosterone propionate was supplied by the Schering Corporation, Limited, in the form of Oreton.
†Fluoxymesterone (Ultandren) was supplied by the Ciba Company of Canada, Ltd.
‡The cyclophosphamide was supplied in the form of Procytox by Frank W. Horner Limited.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

CANADIAN MEDICINE

By well considered schemes of collective investigation, Canadian physicians could soon gather much valuable information respecting the phases of disease to be found in the widely different classes of this community, and in time improve our methods of prevention and cure. But that means organization on the part of the leaders of the profession, and honest, intelligent work on the part of the general profession. By carefully observing and recording his cases, their origin, course and treatment; by viewing them in the light in which they are seen; by having regard to their distribution, and the peculiarities of climate and people, each member of the association and each contributor to its journal may do much towards building up a real Canadian medicine. —Excerpt from editorial, *Canadian Medical Association Journal*, 1: 149, February 1911.

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THE GLOSSO-BUCCAL SYNDROME

THERE can be no reasonable doubt that in recent years there has occurred an explosive technological advance and a burgeoning of intellectual concepts concerning the mysteries of the human body in health and disease. Inherent in such rapid scientific progress is the grave risk that the unprepared and unsuspecting reader of today's medical periodicals may be precipitated into irreversible neurotic depression by his frustrated efforts to keep himself intelligently informed of this avalanche of new developments. Imagine, for instance, the utter humiliation in being forced to confess ignorance of such currently popular conversation pieces as the forbidden clones, Hartnup disease, baggasosis, the Hageman trait, antigenic determinants or the role of self and non-self in immunologic homeostasis!

This state of affairs in itself is serious enough, but quite recently a new threat to the medical journal reader's mental health has insinuated itself into certain well-known and respected periodicals. This sinister development takes the form of what could be termed most appropriately the glosso-buccal syndrome. The following examples are cited with the hope that they may assist journal readers in its early recognition.

It has been manifested in comparatively benign form by the editor of the *Journal of the American Medical Association* in a recent editorial communication in which reference is made to the incurable, hereditary malady *septicemia eohippus* (Gr. *hippos*, horse) which, only a generation ago, was said to have been essentially as stigmatizing as syphilis or atheism.[1]

A more flagrant manifestation of glosso-buccalism, however, is to be found in an even more recent edition of a world-renowned British medical periodical. Therein the wily fox[2] who guides the editorial destinies of the journal concerned (which shall remain respectfully unnamed) has segregated under the heading "VERY SPECIAL ARTICLES", two of the most carefully documented cases of the glosso-buccal syndrome that have come to our attention. The clinical features of this syndrome can best be demonstrated by direct quotations from the articles to which we refer. The first of these, a treatise entitled "Normalcy and the Gamma Efferent System",[3] concerns the structural and physiological organization of the human nervous system and its ability to adapt to the daily stress to which it is subjected. At least this would appear to be the theme of this paper, although further study may be necessary before such a conclusion could be established with finality. Since the references listed in this article are of some significance, and since we have not been able to confirm these in any recognized index of medical literature, the author's own system of reference listing will be adopted in quoting certain passages from this work. In his review of historical events leading to the evolution of the concept of the gamma efferent system, the author states that as early as 1893, Held "demonstrated the presence of an efferent nerve leading from the area of the superior olive to the cochlea.[10] Being educated in the old Viennese tradition,[11] he lost these findings at the Opera-ball in 1894, and it was left for Cajal and Rasmussen to rediscover what is now known as the olivocochlear bundle." Later, in a discussion of disproportionate responses of the gamma efferent system, it is observed that "Studies such as those of Lilly[13] and Meyer show that hallucinations are frequently experienced after removal of the external stimuli by either physical or pharmacological means." The author further cites an interesting, perhaps congenital, example of underactivity of the gamma efferent system in the case recorded by Mahler, a female patient named Lotta who "showed markedly diminished pain sensitivity to the point where one day, out of pure malice, she scorched her lips on a glowing cigar lighter."[18] In the concluding paragraph of this remarkable discourse the author apologizes for having wandered astray, at times, in his discussion, and confesses that "Starting with a neuron, we have jumped in and out of afferent and efferent tracts, with results which unencumbered by data, recall Pirandello's *Cosi e, se vi pare* (It is so, if you think so)."

The second example of glosso-buccalism in this particular journal is in the form of a brief report of original studies on "The Gekochteundebrocheneeierschale Phenomenon".[4] In this study "Six recently delivered enveloped ova (of *Gallus domesticus*) were divided into three experimental groups of two each. On three successive days one group was immersed in cold water and raised to 100° C. for two minutes. Of the six samples, five developed extensive envelope stress patterns involving the escape of protein into the liquid environment."

"Over a further period of three days three batches each of two enveloped ova were heated in the same manner. In each case, before heating, a canalization (by the technique described by Makewater [1959])

was performed in the rounded terminant. The results were remarkable: stress signs were absent and denaturation was absolute."

"Controls canalized in the pointed (as distinct from the rounded) terminant, were consistently deprived of protein to a degree which led to the condition described by Eddelweiss as *hervorgebrochen.*"

In discussing these observations it is astutely noted that "if each end (of the ovum) were equally rounded and was, moreover, equidistant from the other end, it would be impossible to apply successfully the Makewater technique of canalization in more than the appropriate mathematical chance ratio ($p = <$)."

The author quite rightly observes that the importance of these findings cannot be underestimated and presents the conclusion that "If you prick the thick end of a hen's egg, it won't burst when you boil it."

These reports illustrate the insidious manner in which the glosso-buccal syndrome has invaded today's medical literature. They are recorded here because we feel it our duty to draw to the attention of the Journal's readers this current development in medical journalism.

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2. Fox, T. F., Editor, *The Lancet*, 7, Adam St., Adelphi, London W.C.2. Telephone: Temple Bar 7228/9.
3. MENKES, J. H.: *Lancet*, 2: 1394, 1960.
4. MAEGRAITH, B.: *Ibid.*, 2: 1395, 1960.

*10. HELD, H.: *Arch. Anat. Entwicklungsgesch.*, 1893, p. 201. (A most interesting reference. The only copy extant is on the second floor of the medical library of the University of Würzburg. Ring bell and ask for Max.)

*11. STRAUSS, J.: *Wine, Women and Song.*

*13. LILLY, J. (This is a marvellous paper. Someone told me about it at a cocktail party a few weeks ago but I haven't been able to hunt up the reference in time for publication.)

*18. Ronson "Prince Charming", $17.85 F.O.B. New York.

*Editor's Note: These references have been quoted directly from Menkes[3] since they could not be confirmed in existing medical indices.

THE MEDICAL LETTER ON DRUGS AND THERAPEUTICS

THE practice of medicine has been made simultaneously more interesting and more difficult by the flood of new drugs which issue from pharmaceutical houses. As a result of dramatic advances in organic chemistry and pharmacology, coupled with the ingenuity and drive of pharmaceutical manufacturers, several hundred new drugs, or modifications and combinations of old ones, are being marketed each year. Unfortunately many are released before they have been assessed clinically to an adequate degree. Too many reports of trials of new drugs are premature and impressionistic. The psychological forces which may cloud the judgment of those conducting clinical trials are sufficiently potent that one requires several reports by different groups to arrive at a balanced opinion. Those well-trained investigators who have accepted the rather tedious and unpopular task of determining, in a highly critical manner, the usefulness of new drugs, find themselves unable to keep up with the numbers appearing. No one doctor has the time or the training to assess published accounts of every new drug which might usefully be employed in practice. If he reads the latest textbooks of pharmacology and therapeutics he is at least a year behind the times. Although in many cases being at least a year behind the therapeutic times is an excellent position to be in, there are occasions when one wishes an objective, reliable opinion of a drug which has been released recently. Doctors and medical students need brief, accurate, up-to-date information about new drugs. Until recently few postgraduate courses have been devoted to the subject of drug therapy; the publication of journals designed to meet the need is also a recent development. A highly commendable fulfilment of this need has appeared in the form of a brief publication entitled *The Medical Letter on Drugs and Therapeutics.*

It is not surprising, and quite in keeping with the economic philosophy of free enterprise, that drug companies have capitalized on the great profit potential of their new products. Methods of advertising drugs resemble those of other businesses, in some cases using Madison Avenue techniques. Doctors are exposed to seductive pitches about the worth of some pharmaceuticals; persistent repetition keeps the names of certain products and manufacturers before the medical profession. Homes and offices are flooded with a stream of advertising which, so far, we have been powerless to stop. A statement from the report of the Committee on Pharmacy of the Canadian Medical Association, given at the last annual meeting, probably represents accurately the feeling of most doctors. It says, in part, "direct-mail advertising . . . has reached the point where it is nothing more than a nuisance to its recipients". The Committee recommended "to the Pharmaceutical Manufacturers Association that it should be discontinued and the saving passed on to our patients." Although some companies are careful to state in advertisments how a drug acts, its advantages over other compounds and its toxic hazards, too much advertising uses a juvenile format which employs phrases and illustrations to amuse or alarm the reader.

The Medical Letter on Drugs and Therapeutics is a four-page newsletter, published every two weeks by Drug and Therapeutic Information, Inc., 136 East 57th Street, New York 22, New York. It can be read more quickly than the daily newspaper. There is no advertising in this non-profit publication to inhibit the editors in their policy of printing outspokenly candid opinions of new drugs. The brief articles tell in simple language about the validity of therapeutic claims, drugs of choice, side effects and cost to patients. The editorial board consists of distinguished leaders in pharmacology and therapeutics. The doctor who studies this publication (which costs $12.50 per annum) will be kept well informed and can throw the direct-mail

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advertising in the wastepaper basket with a clear conscience. He will approach more closely that wise and witty definition of a good doctor printed long ago in "Poor Richard's Almanac" by Benjamin Franklin: "He's the best physician that knows the worthlessness of the most medicines."

W. B. SPAULDING, M.D.,
Associate Professor of Medicine,
University of Toronto.

CURRENT VIEWS ON RESPIRATORY DISEASES IN THE U.S.S.R.

PRESENT-DAY Russian concepts of the etiology, diagnosis and treatment of diseases of the respiratory system are presented in panoramic review, symposium style, in the October 1960 issue of *Klinicheskaya Meditsina.*

The editorial writer discusses current activities in the study of the pneumoconioses and speculates on the future outlook of such investigations. Emphasis is placed on four principles that are considered fundamental in the study of any patient with this disease: (1) A careful occupational and clinical history should include the details of the subject's environmental and working conditions. (2) Due consideration should be given to the stage of his disease, its natural history and the general functional state of his respiratory, circulatory and other systems. (3) An attempt should be made to assess the degree to which he has compensated for the pneumoconiotic changes, and (4) the study of each patient should be approached on a strictly individual basis.

The advancement of knowledge concerning occupational disease due to inhalation will require improved methods for earlier diagnosis; continuing studies of pathogenesis which will involve biochemical, physiological and morphological techniques of investigation; research in improved methods of active treatment both in the clinic and on experimental animals; more accurate techniques for assessment of the work capacity of patients with these diseases; and a continuing search for, and study of, new forms of pneumoconiosis.

In the opinion of Rabuchin of Moscow, there is still a definite place for therapeutic pneumothorax in the treatment of circumscribed, focal, infiltrative tuberculosis of the lung without involvement of larger bronchi and in the absence of emphysema. He considers that this measure is an important adjuvant to chemotherapy in such cases and recommends that it should be continued for an average of two years. If satisfactory pneumothorax cannot be attained, other means of surgical collapse therapy should be employed.

In discussing the treatment of bronchial asthma, Schwitzer commented on the effectiveness of 5% ephedrine, the subcutaneous injection of 0.3 to 1.0 ml. of 0.1% adrenaline and the inhalation of smoke from "asthma cigarettes". Euphylline, administered intravenously or in the form of an aerosol, is recommended for patients resistant to adrenaline. Cupping, mustard sinapisms, foot baths, and aspirin may be effective in mild cases. The use of morphine is not advocated for the asthmatic patient. In some cases, status asthmaticus has responded satisfactorily following the intravenous administration of 100 ml. of 5% novocaine containing 10 units of ACTH. This author also emphasized the importance of measures designed to "change the patient's state of reactivity". In this category were included autohemotherapy by "microtransfusions" of 50 to 70 ml. every three days, and insulin shock produced by the administration of 40 units of insulin twice daily, especially during an asthmatic attack. Suggestion and other forms of psychotherapy are said to be of benefit in the treatment of asthma, through their influence on "neuroendocrine" factors. Prolonged sleep has not been associated with beneficial results in this disorder and is now considered contraindicated. It was claimed that good results had been obtained in some cases following novocaine blockade of the cervical and abdominal sympathetic nervous pathways. Various forms of physiotherapy, including suberythemal doses of ultraviolet light, diathermy and ultra shortwave therapy, enjoy considerable popularity in the treatment of asthma, as do breathing exercises, with particular emphasis on those involving prolonged expiration. In recent years fatalities associated with severe asthmatic attacks have been observed with increasing frequency. The mechanism of death varies; in some it is due to asphyxia, in others to "central depression". In rare cases, acute right ventricular failure is the cause of death.

Belsky reported the interesting observation that 18 of a group of 25 patients with pleural effusions exhibited dermographism which was appreciably more pronounced over the underlying effusion than on the unaffected side of the chest. The dermographism became more intense as the amount of effusion increased and faded as the pleural fluid was resorbed.

The value of inhalation of oxygen and carbon dioxide in the treatment of patients with chronic pulmonary insufficiency was discussed by Sorinson, and the results of a questionnaire dealing with the effects of smoking on various aspects of health were reported by Slinin. Other papers in the symposium dealt with the work capacity of patients with healed pulmonary tuberculosis; side effects of antituberculosis chemotherapy; hormone therapy for tuberculosis; anthracosis; essential pulmonary hemosiderosis; and pulmonary edema.

It is of interest to note that the majority of these articles are accompanied by short summaries in English, which appears to be gradually gaining wide acceptance as a popular medium for scientific communication, at least among publications devoted to the medical sciences. W.G.

LETTERS TO THE EDITOR

TAXES AND MEDICAL SERVICES

To the Editor:

If 1960 could be considered, as our Editor suggested, a "highly political year",[1] let us make 1961 a "highly enlightening year" from the point of view of the Canadian Medical Association and the Canadian public. First indication of such a period of more rational and logical thinking comes from the publicity already widespread across the country incident to the broad distribution of our statement of policy on medical services insurance, to the release of the second part of the report of the Committee on Prepaid Medical Care, and to the results of the request of the Canadian Medical Association for a Royal Commission on Health Services.

Already the emerging public image of a profession that is up-to-date on today's social thinking, and possessed of ability and willingness to provide the highest quality of medical care on a prepaid basis, should challenge us to more effective objectives.

To get our own thinking straight is the first requirement of a better public relations approach. Unless we as a united profession talk wisely and with objectively accurate argument, we cannot expect either a receptive or an appreciative audience.

We have made a beginning. What comes next? To this writer our most pressing need is a decent vocabulary. We must rid our conversation of all such emotionally charged expressions as "state medicine", "socialized medicine", "winning the battle", "fighting bureaucrats and politicians" and express ourselves ably and well in the matters which we should be so specially trained to discuss. Let us rid our medical parlance and literature, once and for all, of anything and everything which would create in the minds of the public the impression that we are opposed to changes as such. The year 1961 should show that our profession has a thorough and unselfish program of medical services insurance which we are willing and able to implement with the help of, and for the good of, all the Canadian people.

But we should be realistic in our approach. We should enlighten the public in all phases of our thinking. It is long past the time when the profession should use such expressions as "free tuberculosis or cancer care", "free medical care", free hospitalization" and the like. In such sense the word "free" applies only to the service at the time it is rendered and has no relation whatsoever to the specific program involved. In all of our utterances we should grasp every occasion to speak of "tax-supported care and service" of all types. All health services of the type being contemplated will have to be supported in whole or part by taxes—large taxes that will bear heavily on all citizens. We will understand each other much better if we speak to the public and to politicians about "tax-supported programs".

It was a wise head indeed who introduced this term into our Statement of Policy in June 1960.[2]

If the Canadian Medical Association and its leaders, and if the Divisions and their officers are to bring to the Royal Commission on Health Services and to the Canadian people, the basic ideals of quality medical care and their application in practice under any form of economic program for payment of services, the efforts of each and every doctor and his enlightened voice must be presented, united, realistic, honest and unselfish. Our professional status and our long history of service demand this as our minimum individual contribution. Our patients expect our leadership at this time and they have a right to our enlightened guidance.

J. A. McMillan, M.D., C.M.

Charlottetown, P.E.I.

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USE OF WATER SOFTENERS IN HOSPITALS

To the Editor:

I have encountered a problem which should probably be brought to the attention of other persons practising in rural areas where there is no municipal water supply, or where water supplies used in hospitals require softening. During the fall of 1960 a water softener, using zeolite as an adsorbant, was installed in the local Dinsmore Union Hospital, all the water being used in the hospital being routed through the softener. It was noticed that saluretics, such as hydrochlorothiazide, used in the treatment of hypertension and edema of congestive heart failure, etc., were suddenly found to have little or no expected effect. After considering the possible explanations for this phenomenon, of encountering unusual patients, or erratically functioning stocks of drugs, it was recognized that the water softener was converting the water used in the hospital for every purpose into a mild saline solution, and as a result we had all of our hospital patients on a fairly high sodium diet!

Corrective measures have now been taken in the hospital, by routing some of the water directly from the well used to supply the hospital with water to most of the cold water taps in the hospital, and specifically to the kitchen where the meals are prepared. My patients now obtain the usual expected result from administration of saluretics.

I felt that this information was worthy of note in the Journal, inasmuch as the installation of water softeners in hospitals is being considered economically valid in communities around here and perhaps in many other communities in Canada. The facts as noted above should be taken into consideration by the medical staffs and the hospital boards who may be concerned.

David J. Brant, M.D.

Dinsmore, Sask.

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MEDICAL NEWS IN BRIEF

THE WHITE BLOOD CELL COUNT IN COLOURED AND WHITE PEOPLE IN THE ATOMIC ERA

The development of nuclear weapons has caused radioactive pollution of the atmosphere. The fallout is still increasing and, provided no further atomic bombs are used, the peak is expected between 1962 and 1965, especially between 20° and 60° north latitude. It is not yet known whether or not continued exposure to this degree of fallout will have any long-term effects on the human race. Therefore it would be desirable to have simple, inexpensive tests suitable for follow-up examinations on certain biological functions known to be influenced by radiation. The white blood cell count may prove useful in this connection.

Jalcowitz (*Wien. klin. Wchnschr.*, 72: 750, 1960), having noticed a downward trend in the leukocyte count for some years at his private hospital at Porte-au-Prince, Haiti, undertook a statistical evaluation of data on this subject. All patients with febrile illnesses, children under the age of five years and patients with any disorders which might cause a change in the white cell count were excluded. This left 1577 cases, four-fifths of them Negroes and mulattos, and the rest white patients. During the entire period of study the leukocyte counts were all performed by the same person using the same technique and the same instruments.

In 1949 the average leukocyte count was 6461 per c.mm., whereas in 1959 it was 4915, having dropped gradually during the 11 years of observation. The fall was caused by a diminution in the number of granulocytes only. Age and sex had no influence on this phenomenon, but a separate evaluation of the white and the coloured patients showed a greater leukocyte fall in the latter group.

The concomitant rise in radioactive fallout from 0.02×10^{-12} μc./c.c. in 1953 to 0.24×10^{-12} μc./c.c. in 1957 raises the possibility of a causative relationship. This may be a danger signal that should not be overlooked, and the author suggests that more studies of this type be carried out in other parts of the world.

THE FEET AS AN AID IN THE DIFFERENTIAL DIAGNOSIS OF ARTHRITIS

Joints which are affected frequently by arthritis are those of the feet and hands. Though it is well established that the appearance of hands may aid the physician in differentiating the type of arthritis present, it is little recognized that changes seen in the feet may also assist in one's differential diagnosis. With this view in mind, and in the hope that it may arouse interest in an area often neglected, Calabro has outlined the differential features of arthritis in the feet (*Arthritis & Rheumat.*, 3: 435, 1960).

The features of rheumatoid feet include: (1) hallux valgus; (2) bilateral and symmetrical cock-up toes (hammer toes); (3) metatarsal head spread, prolapse and tenderness; (4) thickened and tender Achilles' tendons; (5) associated corns, calluses and bunions, and (6) distinctive calcaneal and metatarsal cystic lesions radiographically.

Feet changes in psoriatic arthropathy may be separated into two types. The classical type ("psoriasis arthropathica") is limited to characteristic nail changes, skin lesions and terminal interphalangeal joint involvement. Radiologically, resorption is limited to the terminal phalanges. A second type ("rheumatoid-like") is associated with the spectrum of features typical of rheumatoid arthritis, including metatarsal and calcaneal cystic lesions on x-ray.

Visible and radiographic tophi characterize chronic tophaceous gout. Hallux rigidus should not be considered diagnostic, since it occurs in less than 5% of gouty subjects and appears more frequently with degenerative joint disease and rheumatoid arthritis.

Though feet derangements of degenerative joint disease are not well defined clinically, the x-ray appearance of narrowing of joint space and sclerosis with osteophytic spurs is distinctive.

Diabetes is by far the most common cause of neuropathic joint disease occurring in the feet. The progressively painless thickening and deformities of the feet are depicted radiographically by a unique attenuation of metatarsal shafts which taper distally, metatarsal head absorption and midtarsal proliferation.

LOCALIZATION OF THE LESION IN MITRAL STENOSIS

The results of phonocardiographic investigation by Petrovsky *et al.* (*Terapevticheskyi Archiv.*, 8: 33, 1960) were correlated with the operative findings in 80 patients with mitral stenosis. The site of maximal intensity of the mitral diastolic murmur was not constant but varied with the type and position of the stenotic lesion. Detailed investigation of 35 of these patients led to the following observations. Differences in the exact site of maximum intensity of the diastolic murmur depend on variations in involvement of the mitral valve. When the anterior commissure is predominantly involved, the murmur is heard best over the mitral area. When stenosis originates in the posterior commissure, the site of maximum intensity of the murmur is at a higher level in the chest and it is transmitted to the axilla. When both commissures are involved and the stenosed opening occupies a central position in the valve, the diastolic murmur is heard best in the upper chest and does not radiate to the axilla. Thus a correlation of the auscultatory findings with those of phonocardiography can aid in accurate localization of the exact site of the stenosing lesion and can assist in elucidation of the detailed pathological changes in the valve, providing the surgeon with important information preparatory to commissurotomy.

(Continued on advertising page 25)

MEDICAL MEETINGS

THE ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

SCIENTIFIC SESSIONS*

COMBINED SESSION: DIVISIONS OF MEDICINE AND SURGERY, SATURDAY, JANUARY 21

Dr. Peter Allen of the University of British Columbia discussed the major aspects of surgical technique and the selection of patients for resection of arteriosclerotic and luetic aneurysms of the thoracic aorta. Six of the 10 patients in the series he described had their general circulation supported by left atrial to femoral artery by-pass through a Sigma motor pump, while the aorta was cross-clamped proximal and distal to the aneurysm. This technique prevented serious hypertension in the proximal aortic segment and hypotension with cord damage distal to the clamp.

Left superior vena cava, a relatively uncommon finding, was present in at least 28 of 799 patients referred for cardiac investigation, including catheterization. In reporting the detailed findings on these patients, *Drs. Fraser, Rossall and Dvorkin* of Edmonton noted a variety of associated anomalies including both cyanotic and acyanotic types of intracardiac lesions, the largest single group of which consisted of malformations of the atrial septum or atrioventricular cushions.

Drs. Callaghan, Couves and Gilmour of Edmonton analyzed their experience in direct-vision repair of atrial septal defects of 40 patients, utilizing extracorporeal circulation and cardiopulmonary bypass with a bubble oxygenator for the first 19 patients, and a rotating disc oxygenator for the last 21.

The features of a case of idiopathic (Fiedler's) giant-cell myocarditis were summarized by *Dr. E. R. Gubbay* of Montreal. The major features of this disorder are progressive heart failure, unremitting disturbances of rhythm and sudden death. Differential diagnosis may be difficult because it may be accompanied by angina-like pain; the electrocardiogram may suggest currents of injury, impending or established myocardial infarction; the serum transaminase may be significantly elevated and aneurysm or rupture of the left ventricle may occur. More or less extensive necrosis of heart muscle is the significant pathological finding. While corticosteroids have not been of definitely established value, their administration in the treatment of this disorder should probably be continued till more data have been accumulated.

Drs. Bigelow, Heimbecker, Sapirstein and Kuyper of Toronto discussed indications for operation, surgical technique and results of follow-up of 20 patients with mitral insufficiency who had been submitted to open heart annuloplasty with cardiac bypass. All had pure or predominant mitral insufficiency. Results of post-operative assessment were highly encouraging.

The results of routine hemodynamic, clinical and pulmonary function studies on 19 patients with mitral disease were reported by *Drs. Palmer, Mills, Gee and Bates* of Montreal. This investigation also included measurement of carbon monoxide diffusing capacity, pulmonary capillary blood volume, diffusing capacity of alveolar membrane and pulmonary compliance. The results were classified in three groups: (1) those with minimal functional disability and close to normal pulmonary capillary blood volume, alveolar membrane diffusion and pulmonary compliance; (2) those with moderate functional impairment, a tendency to pulmonary edema, marked elevation in pulmonary capillary blood volume, decreased alveolar diffusing capacity and below-normal compliance (it was suggested that this group showed the best response in clinical and physiological criteria after mitral surgery); and (3) the most disabled patients with greater decreases in alveolar membrane diffusing capacity and compliance but a return of the pulmonary capillary blood volume to normal.

Dr. N. J. Jackson and Mr. R. Cobbold of Saskatoon described a transistorized electronic unit in which the R wave of the electrocardiogram automatically initiated a sequence of events culminating in the injection of a selected volume of contrast medium through a catheter placed in the root of the aorta, immediately followed by x-ray exposure. This automatic, ECG-activated, coronary injection apparatus may be used both for coronary arteriography and for injection of concentrated fibrinolytic agents in patients with acute coronary thrombosis, without significant concentration of the fibrinolytic drug in the systemic circulation.

Drs. Johnson, Stanford, Quan, Palmer and McGregor of Montreal reported on the effectiveness of a permanent electronic intracardiac pacemaker in controlling Stokes-Adams attacks in a 67-year-old man who had been leading a normal life of retirement without symptoms referable to the cardiovascular system throughout the three-month period since the pacemaker was installed. A catheter electrode was inserted in the right external jugular vein and its tip was placed in the right ventricular cavity. An external electrode was inserted percutaneously in the right anterior chest wall. The stimulus was provided by a Medtronic pacemaker worn on the belt beneath the shirt. The patient was maintained on anticoagulants. The pacemaker permits adjustment of the heart rate as desired without changing other physiological factors. The authors showed a cine strip illustrating this apparatus in action.

DIVISION OF SURGERY

The first session of the Division of Surgery was chaired by Dr. N. C. Delarue.

Dr. C. M. Couves presented the result of work done in the Department of Surgery and the McEachren Laboratory of the University of Alberta on isolation and perfusion techniques in 27 patients with cancer. The drugs used were P.A.M. and T.S.P.A. and their indications were either adjunctive or palliative. Definitive results of adjunctive perfusions will not be known for five to eight years; it may be stated at the present time that palliative perfusions used mainly for pelvic recurrence of tumour are not encouraging. *Dr.*

*For a report of the sessions of the Division of Medicine and of the Gordon Richards Memorial Lecture, see pages 397 to 402, issue of February 18.

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Henderson of Boston pointed out as a comment that relief of pain may be due to some anesthetic property of cytotoxic drugs on nerve endings.

Dr. D. Magner reported on a neoplasm which may well be a newly recognized tumour entity. Testicular adenocarcinomas with clear cells were isolated from 13 infants. All of these tumours were locally invasive, expanding the testis but respecting the tunica albuginea. The histogenesis of the vacuolated cells is still unsettled. Treatment has been by simple orchiectomy with or without radiotherapy. Two more cases were mentioned by *Dr. Collins* in discussion from the audience. It was agreed in the discussion that radical retroperitoneal lymph node dissection from the diaphragm down should be seriously considered when operating for such tumours.

The very topical question of cancer cells in the circulating blood was ably discussed by *Dr. R. C. Long*, representing a group of research workers from the Royal Victoria Hospital (Montreal) and McGill University. Circulating cancer cells were found in the blood of 50% of the patients studied. It appears that regardless of its clinical stage, such cells may be found in each case of carcinoma of the breast, if the technique is accurate and if enough samples of blood are drawn for examination. The prognostic value of this test is therefore nil. The persistence of cancerous cells in the circulating blood for a long period of time (sometimes months after the operation) is of clinical value and may be an indication that further therapy is required. During the interesting discussion which followed the presentation of this paper, the question of false positives was raised, as exemplified by the atypical cells obtained from the stomach of patients with pernicious anemia and in patients with scleroderma. The significance of clumps of cells as opposed to isolated cells was also touched upon.

Dr. S. E. Carroll of the University of Western Ontario pointed out that the crude five-year survival rate of patients with carcinoma of the rectum with venous invasion was 30.4% compared with 48.3% for patients with the same tumour but without venous lesions. The importance of these figures stems from the fact that 11.8% of the 1996 cases studied showed involvement of the veins. This paper was illustrated by interesting slides and gave rise to favourable comments. The youthfulness of the author prompted *Dr. G. E. Moore* to remark that the average age of medical discoverers is 34.

The evaluation of intra-operative blood loss as a guide for blood replacement was studied by *Dr. W. Spoerel* of London, Ont., by means of radioactive iodinated human serum albumin. Using the surface area as a basis for figuring the expected values, he demonstrated from a series of 50 major surgical procedures that a preoperative determination compared to another performed one hour after completion of the operation will supply valuable information for the guidance of replacement therapy. In their comments *Drs. A. R. Dobell and F. N. Gurd* stated that their experience with this method agreed with that of the speaker.

A group from the Montreal General Hospital represented by *Dr. M. N. Lougheed* presented their results of preoperative radiation in bronchogenic carcinoma. It appears from this study of 18 cases that this therapeutic approach improves the resectability rate, provides a safe period during which the patient can be observed, decreases the viability of surgically disseminated tumour emboli and supplies a number of other lesser advantages. During the lively discussion that followed, *Drs. Boyd and Gagnon* both expressed their pessimistic outlook concerning this regimen, the latter stating that what really counts in prognosis is the host's reaction to his tumour. *Drs. Nanson, Grossman, MacNaughton and Simpson* contributed additional comments.

Dr. S. D. Gordon's suggestion of having his paper read by title on account of the late hour was rejected by the Chairman with the support of the audience. It proved a wise decision, as "The Treatment of Rodent Ulcer" was an interesting paper illustrated by excellent slides. This neoplasm which in 90% of cases appears on exposed surfaces accounts for 6% of deaths from carcinoma of the skin. The blue-eyed blonde type is more susceptible than his darker counterpart. The lesion may present as the "greasy doughnut", the "iceberg tumour" or the rare pigmented rodent ulcer. Whereas excision, radiotherapy and electrodessication are acceptable forms of treatment, dermabrasion should never be used. When mutilation will not provide any reasonable expectation of cure, treatment may as well be withheld.

The Friday afternoon session was chaired by *Dr. A. D. McKenzie* of Vancouver and opened with a presentation by *Dr. D. P. Boyd* of the Lahey Clinic in Boston on pseudoembolic phlebitis, also known as phlegmasia cerulea dolens. The severe pain and massive swelling which cause the patient to feel as though his leg would burst are associated with arterial spasm and the syndrome of surgical shock. The process may go on to loss of peripheral pulses, blue mottling and gangrene. Pulmonary embolism may supervene and amputation may be required. The most favourable treatment seems to consist in early institution of epidural block, anticoagulation and intra-arterial injections of antispasmodic drugs. In the course of the discussion, *Dr. F. N. Gurd* wondered why fibrinolysin had not been mentioned as a form of treatment, but it seems that nobody had much experience with it in this field.

The surgical aspect of hyperparathyroidism was described by *Dr. J. A. Palmer* of Toronto. From his experience with 26 cases at the Toronto General Hospital he stated that the neck should be explored through as avascular a field as possible and all four or five glands should be checked for size and colour. The capsule should not be ruptured during removal of the glands. *Dr. J. Balfour* pointed out that to his knowledge renal calculi resulting from hyperparathyroidism were usually bilateral and recurrent; *Dr. W. C. MacKenzie* associated hyperparathyroidism with some psychiatric symptoms.

Dr. L. N. McAninch described his technique of pyelolithotripsy which consists of cracking staghorn stones by means of a renal lithotrite (a special model having been designed for him) and removing the fragments without injury to the renal parenchyma. Small special cassettes are set directly in the wound for radiological control to ensure that all fragments are removed. With the help of proper postoperative medical management the results have been gratifying. *Dr. J. Balfour* pointed out that occasionally patients who harbour renal calculi will go on to develop squamous cell carcinoma of the renal pelvis. *Dr. J. O. Metcalfe*

contributed remarks on the so-called "medical cures" for kidney stones.

Dr. E. M. Nanson reviewed a series of cases that involved the surgical approach to the thoracic inlet. Eight different headings which grouped the conditions to be considered were illustrated by case reports. Complications which may be encountered in this area were outlined. Dr. Nanson's paper will be published in a forthcoming issue of the *Canadian Journal of Surgery*.

The effects of lumbar sympathectomy on the peripheral blood flow, blood gas and electrolyte content as observed in the dog's limbs were presented by *Dr. P. K. Padhi* from the cardio-thoracic unit of Queen's University. *Dr. Padhi and Dr. R. B. Lynn* have been studying the relationship between the return of vascular tone and oxygen saturation in the venous blood of a sympathectomized limb and trying to determine any alterations in the electrolyte content of that blood.

Dr. A. D. McLachlin demonstrated quite clearly and convincingly the importance of venous return in the development of thrombosis. By means of a series of excellent radiological illustrations he showed how thrombi may take origin in valve pockets when stasis is allowed. In a human leg resting horizontally motionless, as is the case at most operations, dye can be observed in venous valve pockets for as long as 27 minutes after injection. Lifting the leg 15° reduces this time lag to 4.8 minutes. If the subject is standing, dye may linger up to 38 minutes; walking eliminates it in 7.6 minutes. It may therefore be concluded that early postoperative ambulation may not be as useful as raising the foot of the bed in the prevention of thrombosis.

In discussing the prognostic value of "benign" discharge from the nipple after local incision, *Dr. V. A. McPherson* recorded that of 1205 patients with breast lesions, 72 (6%) presented with such a symptom associated with intraductal papilloma (41%), duct ectasia (23%), carcinoma (12%), and cystic disease (12%), the remainder being due to rarer lesions. The incidence of malignancy developing in the same breast after local excision was lower than that occurring in the opposite breast after primary excision of a benign lesion. *Dr. N. C. Delarue* underlined the importance of this work in the management of breast disease.

The section of the meeting devoted to the surgery of trauma was chaired by *Dr. J. R. Francis*. It opened with an analysis by *Dr. J. A. McIntyre* of 143 cases of abdominal injuries encountered at St. Joseph's Hospital in Toronto. The study had been undertaken to emphasize the important factors in assessing patients individually. The overall mortality rate resulting from injury of one viscus only was 15.4%; when two or more viscera were involved, the mortality rate rose to 34.5%.

Dr. J. Robichon spoke on experimental and clinical evaluation of tears of the lateral ligament of the ankle. Based on a series of 28 cases in which it was applied, their repair was successful in 27. Inversion stress on the os calcis produces tilt of the talus if the calcaneo-fibular ligament is sectioned. By grading the extent of tilt in three degrees, the author claims to be able to determine the extent of the damage ((1) anterior talofibular ligament only, (2) the same plus anterolateral capsule or (3) plus calcaneo-fibular ligament). The technique of repair advocated impressed some members of the audience as being a somewhat radical approach.

A group from the Department of Experimental Surgery of McGill University presented a progress report on thermographic assessment of burns and frostbite based on the application of a sensitive infra-red scanning device. Early changes in skin temperature after such lesions are recorded graphically and correlations are attempted with tissue losses that ensue. The method seems promising in the hands of these investigators as reported by *Dr. R. N. Lawson*.

The diagnosis and early management of acute traumatic spinal fluid rhinorrhea was discussed by *Dr. R. Fleming*. Sixteen patients with dural tear and communication between the subarachnoid space and the paranasal air sinuses were found in a group of 766 patients with acute head injuries. The leak is best demonstrated when the patient is either lying face down or bending forward when sitting in a chair. The risk of developing meningitis makes early treatment mandatory. Antibiotics and intravenous urea are useful adjuvants in the surgical repair of such lesions.

A most interesting paper on upper femoral resection in paraplegia was contributed by *Dr. F. A. Ducharme* of Ottawa. This procedure practically abolishes spasms, allows sores to be closed easily, releases contractures and permits resumption of chair rehabilitation. Three patients so far have had bilateral resections and all benefited from the operation.

The afternoon closed with two papers devoted to studies with polyurethane foam (from the Toronto Western Hospital and the University of Manitoba). In dog experiments extending over 17 weeks, the material was inserted into the bed of a subperiosteally resected rib. In other experimental fractures, it was found that the material is not of sufficient strength to allow early weight-bearing although it provides some measure of mechanical stability when implanted. Subcutaneously, it elicited minimal foreign body reaction with early fibrous tissue encapsulation. It does not appear to have any adverse effect on callus formation. Both of these papers were interesting interim reports.

With *Dr. E. P. Nonamaker* in the chair, the third session of the Division of Surgery opened with a discussion on spontaneous rupture of the esophagus, ably delivered by *Dr. N. T. McPhedran* of Toronto. The series of nine patients collected by the author included four patients with cerebral lesions and five associated with vomiting. Symptomatology comprised excruciating substernal or epigastric pain, shock and grunting respiration. The sitting position was found by the patients to be the least intolerable posture. All patients had ileus. Radiological signs of pneumonitis and, often, mediastinal or subcutaneous emphysema were also present; lipiodol swallow may establish the diagnosis. Although it is agreed that raised intraesophageal pressure is an important etiological factor, the crucial point may be the rate of pressure rise. Mucosal defects contribute to a large extent to weakening of the esophagus. *Dr. B. M. Grossman* pointed out that alcoholism predisposes to esophageal rupture; this remark was confirmed by the author, who cited a case in which diagnosis was stumbled upon when thoracentesis produced gastric juice with a high content of Scotch whiskey.

Dr. A. G. Fletcher of Miraj, India, described a technique of coloplasty for reconstruction of the cervical esophagus after pharyngo-laryngectomy. The entire right or left colon is mobilized as in the usual technique for coloplasty, preserving the blood supply through the

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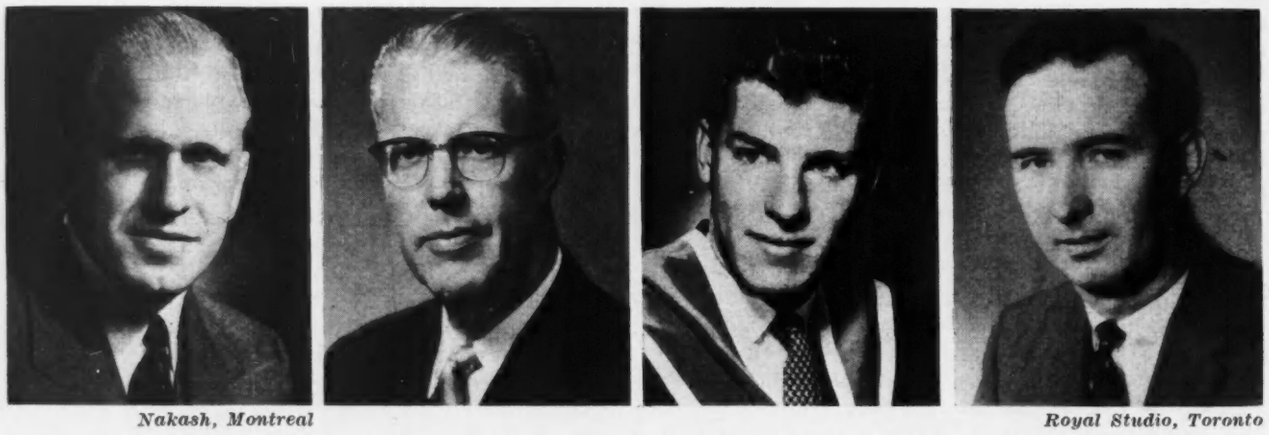

Nakash, Montreal *Royal Studio, Toronto*

Left to right: Dr. Jacques Genest, Montreal, 1961 Lecturer in Medicine; Dr. Walter MacKenzie, Edmonton, 1961 Lecturer in Surgery; Dr. John Orval Parker, Peterborough, Ont., 1961 Medallist in Medicine; and Dr. John Staton Speakman, Toronto, 1961 Medallist in Surgery.

mid colic artery. This segment is passed up retrosternally into the neck where it is joined to the hypopharynx proximally and to the cut edge of the cervical esophagus distally. Good palliative results were obtained by this method in four cases. This presentation elicited favourable comments from *Dr. F. G. Kergin*.

A study of familial multiple polyposis of the colon based on 11 cases from two families was presented by *Dr. T. R. Osler* of Vancouver. The syndrome also includes osteomatosis and soft tissue tumours (mostly epidermoid cysts). Since virtually every member affected will develop carcinoma of the bowel, adequate treatment is imperative; this usually consists of preliminary fulguration of rectal polyps followed by one-stage colectomy and end-to-end ileoproctotomy. *Dr. A. D. McLachlin* commented on the unpredictability of disappearance and recurrence of polyps.

According to *Dr. E. A. MacNaughton's* observations on recurrent volvulus of the sigmoid colon, self-reducing lesions in the younger patient often go unrecognized as a cause of abdominal pain. However, the diagnosis should be borne in mind in cases of recurrent chronic abdominal pain in otherwise healthy individuals. In 13 of 18 patients who were operated upon, a white mesenteric scar was observed and taken as a diagnostic sign that a volvulus had been present. *Dr. R. K. Magee* raised the possibility that some of these cases may be mistaken for localized megacolon, but there were none of this type in the series described in this report.

Based on their experience in the management of five patients, a group from London (Ont.) discussed the surgical problems of annular pancreas in a report presented by *Dr. D. W. B. Johnston*. Possible complications of this rare congenital anomaly include duodenal ulceration, chronic pancreatitis and bowel obstruction. Because of the dangers inherent in direct division of the annulus, short-circuiting procedures are recommended.

Pancreatography was performed in 120 postmortem specimens by *Dr. O. Retzer* of Edmonton, in an attempt to avoid the frequent injury sustained by the accessory duct of Santorini during gastrectomy and to investigate a possible etiology of pancreatitis. Among the interesting conclusions reached in the study was the observation that direct pancreatography in the operating room should be a safe procedure and may be essential in the diagnosis of pancreatic disease, particularly of intrapancreatic duct obstruction.

The role of the skin-fixation factor in wound contraction was studied by *Drs. G. M. Luccioli and H. Rocke Robertson* of Montreal. In the course of experimental work in the rabbit, approximately 80% of 2 x 2 cm. defects in loose-skin areas was covered by wound contraction. In fixed-skin areas, only 40% of identical wounds was covered by contraction in the same period of time. It may therefore be concluded that fixation of the skin inhibits wound contraction.

1961 Lecture in Medicine

The 1961 Lecture in Medicine was delivered by Dr. Jacques Genest, Associate Professor of Medicine, University of Montreal, and Director of Clinical Research, Hôtel-Dieu Hospital, Montreal, on the subject of "Angiotensin, Aldosterone and Hypertension in Humans". Dr. Genest's account of his twelve years of dedicated research in the field of hypertension appears elsewhere in this issue.

1961 Lecture in Surgery

The annual Lecture in Surgery was delivered this year by *Dr. Walter C. MacKenzie*, Professor of Surgery and Dean of the Faculty of Medicine, University of Alberta. For the subject of this address, Dr. MacKenzie had selected the surgery of the pancreas. After having paid tribute to his predecessors in the field, he first discussed the etiology of recurrent pancreatitis. Islet cell lesions were then considered in relation to surgery. The final portion of the lecture dealt with other neoplasms of the pancreas. With a rapid, clear and incisive delivery, the lecturer gave an excellent account of the problem. Pertinent case reports and slides of high artistic quality enhanced his presentation. This paper will be published *in extenso* in a forthcoming issue of the *Canadian Journal of Surgery*.

The Annual Award in Medicine

Dr. John Orval Parker of Peterborough, Ontario, reported on his studies of "Quantitative Radiocardiography" which were carried out at the Cardiopulmonary Laboratory of the Columbia University Division, Bellevue Hospital, New York, and for which the 1961 Medal of the Royal College of Physicians of Canada was awarded.

This procedure provides a technique for the measurement of cardiac output, ventricular volume, and pulmonary blood volume. After the injection of radioactive iodine-labelled serum albumin (RISA), or krypton-85, the isotopes can be traced through the vessels and cardiac chambers by means of an external counting apparatus over the chest wall. The resulting record is referred to as a "total radiocardiogram". By varying the site of injection of the tracer, individual cardiac chambers and the great vessels can be studied by means of "selective radiocardiograms".

Krypton-85 is a poorly soluble gaseous isotope. When injected into the venous circulation, 95% settles out in the pulmonary capillary bed with the first heart cycle after injection, providing a means for intensive studies of pulmonary capillary circulation.

Quantitative radiocardiography has provided a new approach to the hitherto unexplored field of pressure-volume relations in the cardiopulmonary circulation. It affords a means for (1) measurement of cardiac output by indicator dilution technique; by selective radiocardiography the output of each ventricle can be measured: (2) calculation of ventricular volume: and (3) calculation of minimal and true pulmonary blood volumes.

Apex Photos, Ottawa

President Thompson with the platform party, comprising the members of the College Council and recipients of honorary awards, on the occasion of the annual Convocation.

THE ANNUAL AWARD IN SURGERY

Dr. John Staton Speakman of Toronto, 1961 Medallist of the Royal College of Surgeons of Canada, presented a report of his studies on the structure of the trabecular meshwork and corneal endothelium in relation to the problem of resistance to outflow in open angle glaucoma. This report will be published in detail in a later issue of the Journal.

CONVOCATION

The annual convocation was held in the Ballroom of the Château Laurier on Friday evening, January 20, when 174 new Fellows were admitted to the College.

Those in the Division of Medicine were presented to the President by Dr. James H. Graham, Secretary of the College. Dr. W. G. Beattie, Honorary Assistant Secretary, presented the Fellows in the Division of Surgery.

His Excellency Major-General Georges Vanier, Governor General of Canada, was presented to the President by Dr. Charles Hébert, Vice-President, Division of Surgery, for conferral of Honorary Fellowship in the College. Honorary Fellowships were conferred upon Sir Walter Mercer of Edinburgh, who was presented by Dr. R. I. Harris; and Mr. R. S. McLaughlin, Chairman of the Board of General Motors of Canada, presented *in absentia* by Professor A. L. Chute of Toronto.

The Medal of the Royal College of Physicians was presented to Dr. John Orval Parker of Peter-

Dominion-Wide, Ottawa

Dr. Thompson congratulates His Excellency Major-General Georges P. Vanier, D.S.O., M.C., C.D., Governor General of Canada, on his election to Honorary Fellowship.

Apex Photos, Ottawa

Sir Walter Mercer of Edinburgh, at the Convocation ceremonies during which he was made an Honorary Fellow of the College.

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Dominion-Wide, Ottawa

The Right Hon. John G. Diefenbaker with officers and Fellows of the College, on the occasion of the opening of the new College headquarters at 74 Stanley Avenue, Ottawa. From left to right: The President, Dr. Donald A. Thompson of Bathurst, N.B.; the Prime Minister; Dr. Walter MacKenzie, Edmonton, 1961 Lecturer in Surgery; Dr. Frank Patterson, Vancouver; Dr. Donald Webster, Montreal; Dr. K. T. MacFarlane, Montreal; and the Honorary Assistant Secretary, Dr. W. Gordon Beattie, Ottawa.

borough, who was introduced by Dr. Malcolm Brown, and the Medal of the Royal College of Surgeons was presented to Dr. John Staton Speakman of Toronto, introduced by Dr. P. E. Ireland. Diplomas were awarded to Dr. Jacques Genest of Montreal, 1961 Lecturer in Medicine, and Dean Walter MacKenzie of Edmonton, 1961 Lecturer in Surgery.

In addition to the members of the College Executive and Council, and the recipients of Honorary Fellowship, the platform party included Dr. Chester Keefer, representing the American College of Physicians as President of that body, Dr. C. C. Higgins, representing the American College of Surgeons as its First Vice-President, and Dr. C. P. Hodgkinson, representing the American College of Obstetricians and Gynecologists as its President.

Following the Convocation, a reception in honour of the new Fellows was held in the Drawing Room of the Château.

Reports of the two symposia, "Some Interesting Aspects of Environmental Medicine" and "The Irradiation Hazard in Canada", will conclude this account of the Royal College meeting and will be published in the issue of March 4.

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

1960 CERTIFICATION EXAMINATIONS

The list of candidates who were successful in the 1960 Certification examinations in the various specialties will be published in instalments in successive issues of the Journal.

Listed below are the names of those who were successful in the specialties of Anesthesia, Dermatology, Internal Medicine, Neurology and Pediatrics.

SPECIALTY OF ANESTHESIA (54)

Name and date of graduation	*Address*
BAK, ZONKO M.D.(Toronto) 1954	92 Rivercrest Road, Toronto 9, Ont.
BARR, MARGARET NINA M.B., Ch.B.(Edinburgh) 1951	Department of Anesthesia, Saint John General Hospital, Saint John, N.B.
BENTHAM, WILLIAM HARRY M.D., C.M.(McGill) 1955	24 Bendale Boulevard, Scarborough, Ont.
BLAKE-KNOX, PETER ERNEST A. M.B., B.Ch., B.A.O. (Trinity College, Dublin) 1950	Hammond Plains Road, Bedford, N.S.
BORG, FRANCIS XAVIER M.D.(Royal Malta Univ.) 1949	3564 Dufferin Street, Downsview, Ont.
BORIGHT, ROBERT RAILTON M.D., C.M.(McGill) 1944	4068 Grey Avenue, Montreal 28, Que.
BOWMAN, HELEN COOPER M.B., Ch.B.(Glasgow) 1950	266 St. Laurent Street, Rosemere, Que.
BOYER, DONALD EUGENE M.D.(Toronto) 1954	1535 Westbrook Drive, Peterborough, Ont.
CALDWELL, DOUGLAS YOUNG M.D.(Toronto) 1952	149 Three Valleys Drive, Don Mills, Ont.
CHATTERJEE, KAMAKHYAPRASAD M.B., B.S.(Calcutta) 1952	309 Crestview, Ottawa 1, Ont.
CHORLEY, GORDON EWART M.B., B.S.(London) 1950	14635 - 93rd Avenue, Edmonton, Alta.
CLEMENT, GEORGE FRANKLIN M.D.(Western Ontario) 1952	2250 Haines Road, Port Credit, Ont.
COCHRANE, WILLIAM HULL M.B., B.Ch., B.A.O. (Queen's, Belfast) 1949	14503 - 84th Avenue, Edmonton, Alta.
COGGINS, BRIAN HEATON M.D.(Toronto) 1955	8 Tetbury Crescent, Parkway West, Don Mills, Ont.
CRAYTHORNE, NORMAN WILLIAM B. M.B., B.Ch.,(Queen's, Belfast) 1954	30 Sheraton Drive, Apt. 9, Montreal West, Que.

DRYSDALE, ALAN ALASTAIR MACD. M.D., C.M.(Dalhousie) 1955	12 Ford Street, Fairview, Halifax County, N.S.
DUGGAN, FRANCIS ALOYSIUS M.D.(Toronto) 1945	56 Stormont Avenue, Kingston, Ont.
DYCKHOFF, PAULINE RACHEL M.B., Ch.B.(Manchester) 1953	Department of Anesthesia, Royal Victoria Hospital, Montreal 2, Que.
GAGLIANO, ANTHONY M.D.(Messina Univ.) 1949	356 Dudley Avenue, North Bay, Ont.
GARLAND, JAMES MOFFAT BOYD M.B., Ch.B.(Glasgow) 1951	304 Westdale Avenue, Apt. 11, Kingston, Ont.
GILES, ROY CHARLES M.B., B.S.(London) 1953	The Children's Hospital, Bannatyne Avenue, Winnipeg 3, Man.
GOODHALL, PATRICIA OLIVE M.B., Ch.B.(Liverpool) 1954	409 - 11th Avenue N.E., Calgary, Alta.
HAGEN, JOHN MARTIN M.B., Ch.B.(Edinburgh) 1947	University of Alberta Hospital, Edmonton, Alta.
HAMELIN, LOUIS-PAUL M.D.(Laval) 1955	2825, boulevard du Carmel, Trois-Rivières, Que.
HAYAKAWA, JOE M.D.(Manitoba) 1955	671 St. Mary's Road, South Bend Apartment, Winnipeg 3, Man.
HEBERT, CLAUDE D. M.D.(Laval) 1956	Hôpital Laval, 2725 Chemin Ste-Foy, Quebec 10, Que.
HORNE, GORDON MCINTYRE M.D.(Toronto) 1954	48 Eccleston Drive, Apt. 215, Toronto 16, Ont.
HUGHES, EDWARD NOEL M.D.(Toronto) 1947	2175 Kendal Avenue, Victoria, B.C.
JOBIDON, ALFRED M.D.(Laval) 1951	2352, rue Choquette, Quebec, Que.
JOHANNESSON, THORBERG M.D.(Manitoba) 1945	763 Renfrew Street, Winnipeg 9, Man.
KEIL, ALAN MCLEAN M.B., B.Chir.(Cantab.) 1954	25L Spruce Cliff Apartments, Hemlock Crescent, Calgary, Alta.
KRYT, MARIA M.D.(Brussels) 1952	355 Castlefield Avenue, Toronto 12, Ont.
LAVOIE, JOSEPH GEORGES GÉRARD M.D.(Laval) 1955	Département de l'Anesthésie, Hôpital Maisonneuve, 5415, boul. de l'Assomption, Montreal, Que.
LAYCRAFT, GEORGE HAROLD M.D.(Alberta) 1953	Associated Anaesthetists of Regina, 1004 McCallum Hill Building, Regina, Sask.
LUNDQUIST, AHTI SVEN MATHIAS M.D.(Toronto) 1953	878 Kawartha Drive, Peterborough, Ont.
MATHESON, DONALD IRWIN M.D.(Toronto) 1955	12 Glenwood Crescent, Toronto 16, Ont.
OTTON, PAUL EDWARD M.D.(Western Ontario) 1954	5267 Prince of Wales Street, Montreal, Que.
PARANT, FRANCOIS M.D.(Laval) 1956	83, avenue Bon Air, Ste-Foy, Quebec 10, Que.
PARMENTER, ELLICE AGNES M.B., Ch.B.(St. Andrews) 1944	108 Glenvale Boulevard, Leaside, Toronto 17, Ont.
PATOINE, JEAN-GUY M.D.(Laval) 1952	166 est, St-François, Québec 2, Que.
PEISLEY, HAZEL NORMA M.B., B.S.(Sydney, Australia) 1951	95 Le Marchand Road, St. John's, Nfld.
PETRASEK, ANTHONY M.D.(Toronto) 1953	3440 Decelles Place, Apt. 201, Montreal, Que.
PETROVICH, EDWARD M.D.(Toronto) 1955	4404 Pt. Comfort Drive, Akron 19, Ohio, U.S.A.
POIRIER, FLORIAN LAURENT M.D.(Laval) 1951	19, Place Philippe, Apt. 1, Ste-Foy, Quebec 10, Que.
READY, NORRIS HAMILTON M.D., C.M.(Queen's) 1955	809 Dunlevie Avenue, Ottawa 3, Ont.
RENSAA, MARGARET ALICE M.D.(Alberta) 1955	Montreal Children's Hospital, 2300 Tupper Street, Montreal, Que.
SCREECH, GUY M.R.C.S.(Eng.), L.R.C.P.(Lond.) 1952	1524 Argyle Avenue, West Vancouver, B.C.
SKINNER, LESLIE CLARK M.B., Ch.B.(Aberdeen, Scotland) 1950	2701 Regina Avenue, Regina, Sask.
SLOAN, IAN ALEXANDER M.B., Ch.B.(Cape Town) 1953	65 Broadway Avenue (2210), Toronto 12, Ont.
SMITH, JOHN ARNOLD M.D., C.M.(Dalhousie) 1955	Box 810, Windsor, N.S.
TENCH, JOHN FRANCIS M.D.(Toronto) 1952	2035 Malbrook Road, Oakville, Ont.
WALKER, DONALD ANDREW M.D.(Western Ontario) 1951	Department of Anesthesia, University of California Medical Center, San Francisco 22, Calif., U.S.A.
WILLIAMS, FLOYD GEORGE M.D.(Alberta) 1952	1725 Grand Boulevard, North Vancouver, B.C.
YORK, JOHN EDWARD M.R.C.S.(Eng.), L.R.C.P.(Lond.) 1952	Department of Anesthesia, Toronto General Hospital, Toronto, Ont.

SPECIALTY OF DERMATOLOGY (5)

FLORENCE, RALPH M.D.(Toronto) 1955	11 Wilket Road, Willowdale, Ont.
GRANT, DOUGLAS JAMES M.D.(Western Ontario) 1955	28 Weber Street West, Kitchener, Ont.
LESTER, MARVIN GILBERT M.D.(Toronto) 1955	99 Avenue Road, Suite 505, Toronto, Ont.
MERCANTINI, EDWARD STANLEY M.D.(Ottawa) 1955	339 MacLaren Street, Ottawa 4, Ont.
TRINCHAN, ANGEL M.D.(Zaragoza Univ., Spain) 1954	5 Elm Avenue, Apt. 401, Toronto 5, Ont.

SPECIALTY OF INTERNAL MEDICINE (78)

AMIES, DAVID RUSSELL M.B., B.Ch.(Witwatersrand) 1952	6712–112th Street, Edmonton, Alta.
ANDERSON, CAMERON DEWAR M.D.(Toronto) 1955	1228 Kildare Road, Windsor, Ont.
BALTZAN, MARCEL ALTER M.D., C.M.(McGill) 1953	404–408 MacMillan Bldg., Saskatoon, Sask.
BAUGH, CHARLES WILLIAM M.D., C.M.(Queen's) 1953	2610 Clarence Avenue, Saskatoon, Sask.
BAYLEY, THEODORE ARNOLD M.D.(Toronto) 1955	St. Michael's Hospital, 30 Bond Street, Toronto, Ont.
BAYNE, JAMES RONALD DOUGLAS M.D., C.M.(McGill) 1947	6 Winchester Avenue, Westmount 6, Que.
BECK, ROBERT NEIL M.B., B.Ch., B.A.O. (Queen's, Belfast) 1948	1604 Main Street, Apt. 1, Saskatoon, Sask.
BELLEMARE, JOSEPH EDMOND HENRI M.D.(Montreal) 1955	1020 est, rue Sherbrooke, Montreal 24, Que.

BERRY, HENRY M.D.(Toronto) 1954	278 Riverside Drive, Toronto 3, Ont.
BLAU, ALEXANDER M.D.(Royal Univ. of Bologna, Italy) 1939	605 Bloor Street West, Toronto, Ont.
BLOOM, HOWARD WILLIAM M.D.(Toronto) 1955	58 Wembley Road, Toronto 10, Ont.
BRIGGS, ALICE ETHELDREDA M.D.(Toronto) 1955	937 Avenue Road, Toronto 7, Ont.
BRODER, IRVIN M.D.(Toronto) 1955	1288 Rosewood Street, Ann Arbor, Mich., U.S.A.
BURGESS, FREDERICK JOSEPH M.D.(Manitoba) 1950	500 Cordova Street, Winnipeg 10, Man.
CAIRNS, JOSEPH MAY M.D., C.M.(Dalhousie) 1954	3 Walton Drive, Armdale, Halifax, N.S.
CHANG, JAMES CHI M.B., B.S.(Shanghai) 1944	c/o Dr. Louis Lasagna, Johns Hopkins Hospital, Baltimore 5, Md., U.S.A.
COGLON, RUSSELL BARTON M.D.(Alberta) 1954	422 Roehampton Avenue, Toronto 12, Ont.
COOPER, DONALD ASHLEY M.D.(British Columbia) 1955	1820 Grand Marais West, Windsor, Ont.
DEMERS, PERCY THOMAS HENRY M.D.(Ottawa) 1955	1304 Wyandotte Street, Riverside, Ont.
DESAUTELS, SYLVIO M.D.(Montreal) 1951	3849, rue Saint-Hubert, Montreal, Que.
DONEVAN, RICHARD EDGAR M.D., C.M.(Queen's) 1954	3495 Ridgewood, Apt. 104, Montreal, Que.
ELLIOTT, ALVIN JOHN M.D.(Manitoba) 1950	713–22nd Street, Brandon, Man.
EPSTEIN, HANS HAROLD M.D., C.M.(Dalhousie) 1956	457 Mansfield Street, Lancaster, N.B.
EWART, WILLIAM BISSETT M.D.(Manitoba) 1952	948 McMillan, Winnipeg 9, Man.
FIELDS, HAROLD M.D.(Toronto) 1953	100 Gloucester Street, Apt. 1010, Toronto, Ont.
FISHMAN, JOSEPH M.D., C.M.(McGill) 1954	Seton Hall College of Medicine, Jersey City Medical Center, Jersey City 4, N.J., U.S.A.
FITZGIBBON, GERALD MICHAEL L.R.C.P.I., L.R.C.S.I. (Dublin) 1952	Department of Medicine, Canadian Forces Hospital, Kingston, Ont.
FOERSTER, DARRYL KEMP M.D.(Toronto) 1951	383 Ellis Street, Penticton, B.C.
GIGUERE, BERTRAND M.D.(Laval) 1953	Hôpital Reine-Marie des Anciens Combattants, Chemin de la Reine-Marie, Montreal, Que.
GILLIES, RICHARD ROBLIN M.D., C.M.(Queen's) 1955	3550 Ridgewood Ave., Apt. 24, Montreal 26, Que.
GORDON, DUNCAN ALEXANDER M.D.(Toronto) 1955	Royal Victoria Hospital, Montreal 2, Que.
GORESKY, CARL ARTHUR M.D., C.M.(McGill) 1955	5050 Randall Avenue, Montreal 29, Que.
GOULET, YVON M.D.(Montreal) 1955	10440, rue d'Auteuil, Montreal, Que.
HALMOS, VERONICA M.D.(Budapest) 1953	66 Spadina Road, Apt. 1007, Toronto 4, Ont.
HENDERSON, JOHN ASHTON MAITHER M.B., Ch.B.(Manchester) 1952	Mountain Sanatorium, Hamilton, Ont.
HENSCHEL, ERNEST OSCAR M.D.(Charles Univ., Prague) 1945	4709 N. Cramer Street, Milwaukee 11, Wis., U.S.A.
HERBERT, FRANK ALEXANDER M.D.(Manitoba) 1955	The New England Center Hospital, Harrison Ave. and Bennet Street, Boston 11, Mass., U.S.A.
HOLMES, IAN HUGH M.D.(Manitoba) 1953	7725–111th Street, Edmonton, Alta.
JEFFRIES, ROY CHARLES M.D.(British Columbia) 1954	Suite 814, 750 West Broadway, Vancouver 9, B.C.
JOHNSON, RICHARD WESLEY M.D., C.M.(Queen's) 1955	11 Villaire Avenue, Riverside, Ont.
KOMAROMI, GABOR M.D.(Budapest) 1949	6705 De Vimy Avenue, Montreal, Que.
KORMAN, IRVINE ALLEN M.D.(Toronto) 1955	10 Baintree Street E., Downsview, Ont.
KREUTZ, DONALD MELVIN M.D.(Alberta) 1950	1085 Apolydor Avenue, Ottawa 1, Ont.
KUHN, IRVIN NELSON M.D.(College of Medical Evangelists) 1955	560 Finch Avenue West, Willowdale, Ont.
LACOMBE, MICHEL M.D.(Montreal) 1955	8472, Place Bellefontaine, Ville d'Anjou, Montreal, Que.
LAFLAME, RAYMOND M.D.(Laval) 1956	505 est, Grande-Allée, Quebec, Que.
LEWIS, THOMAS HENRY CHRISTOPHER M.B., B.Ch.(Oxford) 1949	Pacific Building, 1665 West Broadway, Vancouver, B.C.
LEZNOFF, ARTHUR M.D., C.M.(McGill) 1955	610 Dawson Avenue, Town of Mount Royal, Que.
MACDONALD, AUSTIN ALEXANDER M.D., C.M.(Dalhousie) 1942	Neil's Harbour, Victoria County, N.S.
MACDONALD, WALTER CHARLTON M.D.(British Columbia) 1955	University of Washington School of Medicine, Department of Medicine, Seattle 5, Wash., U.S.A.
MACKAY, BRUCE KITCHENER M.D.(Toronto) 1941	299 St. Paul West, Kamloops, B.C.
MACLACHLAN, DAVID OWEN M.D., C.M.(Queen's) 1955	294 Wortley Road, London, Ont.
MALYON, MORLEY HART, M.D.(Toronto) 1955	23 Lionel Heights Crescent, Don Mills, Ont.
MASON, WILLIAM EDWARD HALTON M.D., C.M.(McGill) 1951	3465 Côte des Neiges, Suite 81, Montreal, Que.
MEAKIN, JAMES WILLIAM M.D., C.M.(Queen's) 1953	2 Grandstand Place, Apt. 405, Toronto 17, Ont.
MONTGOMERY, DONALD BATES M.D.(Toronto) 1954	169 Glen Road, Toronto 5, Ont.
NADEAU, PIERRE M.D.(Montreal) 1954	507, rue Querbes, Montreal, Que.
NEWMAN, MICHAEL JOHN DAVID M.B., B.Ch.(Cambridge) 1950	1286 Wolseley Avenue, Winnipeg 10, Man.
NOBLE, EDWARD JOHN GOULD M.D.(Toronto) 1956	219 College Street, Apt. 346, Toronto, Ont.
POURBAIX, WILLIAM EUGENE JOSEPH M.D.(Alberta) 1948	Suite 6, Lemarchand Mansion, Edmonton, Alta.
PRICE, JOHN DAVID EWART M.D., C.M.(McGill) 1954	The G. F. Strong Laboratory for Medical Research, 10th and Heather Streets, Vancouver, B.C.
PROKIPCHUK, EDWARD JAMES M.D.(Western Ontario) 1954	2160 Weston Road, Weston, Ont.

PROULX, ANDRÉ M.D.(Montreal) 1951	3423, rue St-Denis, Montreal, Que.
QUENNEVILLE, JEAN GUY M.D.(Montreal) 1954	10617 Rancourt, Montreal 12, Que.
ROY, JULES DALY M.D.(Laval) 1953	62 Boulevard Taché, Hull, Que.
SAUCIER, GUY M.D.(Laval) 1955	2536, Place de Monceaux, Sillery, Quebec, Que.
SHERBANIUK, RICHARD WILLIAM M.D.(Alberta) 1952	6706–110 Street, Edmonton, Alta.
SNIDAL, DANIEL PETER M.D.(Manitoba) 1952	Respiratory Laboratory, St. Boniface Hospital, St. Boniface, Man.
SOLYMAR, JENO M.D.(Pazmany Peter Univ., Budapest) 1949	3350 Linton Avenue, Apt. 204, Montreal, Que.
SPURRELL, PIERCE AUGUSTUS M.D., C.M.(Dalhousie) 1953	1430–4th Avenue S.W., Rochester, Minn., U.S.A.
THIBERT, FLORENT M.D.(Montreal) 1954	6346–26ème avenue, Rosemount, Montreal, Que.
TRASK, BEVERLEY CAMPBELL M.D., C.M.(Dalhousie) 1955	5 Cartaret Street, Halifax, N.S.
VALBERG, LESLIE STEPHEN M.D., C.M.(Queen's) 1954	Etherington Hall, Queen's University, Kingston, Ont.
VINCENT, MERVILLE OULTON M.D., C.M.(Dalhousie) 1955	Homewood Sanitarium, Guelph, Ont.
WALTERS, WILLIAM CHESLEY M.D., C.M.(McGill) 1953	Suite 5, Medical Arts Bldg., 539 Cassells Street, North Bay, Ont.
WEIR, JAMES RAMSAY M.D.(Alberta) 1953	The Smith Clinic, 4815–51st Street, Camrose, Alta.
WOODWARK, GEORGE MILLINGTON M.R.C.S.(Eng.), L.R.C.P.(Lond.) 1947	240 Medical Arts Building, 1105 Pandora Avenue, Victoria, B.C.
YACHNIN, IRVING M.D.(Montreal) 1956	2945 Somerset Avenue, Ville St-Laurent, Que.

SPECIALTY OF NEUROLOGY (5)

ASHENHURST, EDWARD MACLAINE M.B., B.Ch., B.A.O.(Queen's, Belfast) 1953	1 Fraser Crescent, Saskatoon, Sask.
BARBEAU, ANDRÉ M.D.(Montreal) 1956	4635 Clanranald, Montreal, Que.
GUEST, MARGARET MAY M. M.D.(British Columbia) 1954	1536 Victoria Avenue, Regina, Sask.
HUMPHREY, JOHN GILCHRIST M.D.(Toronto) 1954	Suite 3, 35 Leacrest Road, Toronto 17, Ont.
RAMSAY, FRANCIS WILLIAM M.D.(Alberta) 1954	523 Erie Street S.E., Minneapolis 14, Minn., U.S.A.

SPECIALTY OF PEDIATRICS (29)

AFTAHI, FARHANG M.D.(Tehran Univ., Iran) 1955	Camp Hill Hospital, Halifax, N.S.
BENJAMIN, PETER M.D., C.M.(McGill) 1955	240 St. Aubin Street, St. Laurent, Que.
BOYLE, MARJORY HELENA M.B., B.Ch., B.A.O. (Queen's, Belfast) 1955	Ambassador Hotel, Apt. 205, Cambridge, Mass., U.S.A.
BRAUDO, MICHAEL M.B., Ch.B.(Witwatersrand) 1950	The Hospital for Sick Children, 555 University Avenue, Toronto 2, Ont.
CHIN, WILFRED CONSTANTINE M.D., C.M.(McGill) 1954	Mayo Clinic, Rochester, Minn., U.S.A.
DAVIES, HAROLD LLEWELLYN M.D.(Manitoba) 1946	121 Enfield, Norwood, Man.
DRUMMOND, KEITH NEWTON M.D., C.M.(McGill) 1955	300 Dowling Avenue North, Minneapolis 12, Minn., U.S.A.
DUPAL, MARIE-FRANCE ISABELLA M.D.(Université de Louvain, Belgium) 1955	2505 Maplewood, Apt. 310, Montreal, Que.
GIGUERE, JOSEPH PAUL HUBERT M.D.(Laval) 1956	729, rue Bernard, Val Martin, Montreal 40, Que.
GLASS, IRVING HOWARD JACOB M.D.(Toronto) 1955	The Children's Hospital Elland and Bethesda Aves., Cincinnati 29, Ohio, U.S.A.
HILL, ROBERT HUNTER M.A., B.M., B.Ch.(Oxon.) 1950	7137 Arbutus Street, Vancouver, B.C.
JOHNSON, ELIZABETH MARGERY M.B., Ch.B.(Liverpool) 1948	4961 Collingwood Street, Vancouver, B.C.
KOBLENZER, PETER JOHANN M.B., B.S.(London) 1951	Medical Arts Building, Port Arthur, Ont.
KOZNER, ALICE SUZANNE M.D.(Toronto) 1955	92 Latimer Avenue, Toronto 12, Ont.
LANGDON, WILLIAM ARTHUR M.D.(Western Ontario) 1954	356 McKeon Avenue, London, Ont.
MACMILLAN, ANGUS BAXTER M.D., C.M.(Queen's) 1955	302 Medical Arts Building, 1 Young Street, Hamilton, Ont.
NATHAN, MAX TAYLOR M.D.(Western Ontario) 1955	104 Thornton Road, Chestnut Hill 67, Boston, Mass., U.S.A.
NOLIN, GAÉTAN M.D.(Montreal) 1951	8415, rue Saint-Denis, Montreal, Que.
PARKER, KENNETH ROSS M.D., C.M.(Dalhousie) 1956	The Polyclinic, 170-172 Fitzroy Street, Charlottetown, P.E.I.
QUESNEL, BERNARD M.D.(Montreal) 1956	1420, Le Caron, Apt. 3, Montreal 20, Que.
RIGG, JOHN MICHAEL M.B., B.Chir.(Cambridge) 1952	3195 Granville Street, Suite 106, Vancouver 9, B.C.
SHAW, WILLIAM HAROLD M.D.(Toronto) 1955	219 College Street, Apt. 316, Toronto 2B, Ont.
SOUCY, C. ANDRÉ M.D.(Montreal) 1956	Hôpital Ste-Justine, 3175, chemin Ste-Catherine, Montreal, Que.
SZALAY, GLENN COLEMAN M.D.(Manitoba) 1956	755 Centennial Avenue, River Heights, Winnipeg, Man.
THERIEN, BERNARD M.D.(Montreal) 1955	825 sud, rue Belvédère, Sherbrooke, Que.
WEBER, JAMES LOUIS M.D.(Western Ontario) 1955	Hospital for Sick Children, University Avenue, Toronto, Ont.
WEIDMAN, MARTIN LYON M.D.(Manitoba) 1954	"The Park Towers", 2300 Portage Avenue, Ste. 203, Winnipeg, Man.
WHALEY, WILLIAM JOHN M.D., C.M.(Queen's) 1955	9 Margaret Avenue, Kitchener, Ont.
WILSON, WILLIAM MORTIMER M.D.(Toronto) 1955	The Children's Hospital, 17th Street at Livingston Park, Columbus, Ohio, U.S.A.

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Canadian Government Travel Bureau, Ottawa

Visitors view Montreal from the lookout atop Mount Royal.

COME TO MONTREAL! FOR THE 94th ANNUAL MEETING OF THE CANADIAN MEDICAL ASSOCIATION JUNE 19-23, 1961

THE SCIENTIFIC PROGRAM

For some months the Central and Local Program Committees of the C.M.A. have been concentrating on a Scientific Program designed to acquaint general practitioners with new developments in diagnosis and treatment. These Teaching Sessions will commence on Tuesday morning, June 20, and will continue throughout most of the following three days. As they are in the nature of refresher courses they will embrace panel discussions on medicine, surgery, pediatrics, anesthesia, obstetrics and gynecology.

The General Sessions on Wednesday and Thursday will include three special speakers in medicine, anesthesia and psychiatry. On Thursday morning, the Lister Oration will be presented by Dr. Hugo Rosenqvist, distinguished surgeon-in-chief of the South Hospital, Stockholm, Sweden. Other General Session speakers will include: Dr. Charles M. Fisher, Department of Neurology, Massachusetts General Hospital; Dr. LeRoy D. Vandam, Department of Anesthesiology, Peter Bent Brigham Hospital, Boston; and Dr. D. Ewen Cameron, Allan Memorial Institute, Montreal. Friday, June 23, has been set aside as Medical Economics day, which will include a number of addresses and panel discussions on medical services insurance and other economic matters of topical interest. At this time, the Hon. Emmett M. Hall, Chief Justice of the Province of Saskatchewan, will speak on "The Role of the Royal Commission on Health Services". Chief Justice Hall was recently named Chairman of the Royal Commission on Health Services, by Prime Minister Diefenbaker. On the same program, Dr. T. J. Quintin, a member of the C.M.A. Executive, will talk on "Health Insurance in Australia"; and Dr. Hugo Rosenqvist will speak on the same subject insofar as Sweden is concerned. Other medical economics topics will include "Government and Medicine" and "Existing Deficiencies in Health Services – the Saskatchewan Experience". Another Scientific Program feature will be the showing of several medical films dealing with clinical topics.

THE SOCIAL PROGRAM

The Planning Committees in Montreal have also arranged a number of interesting social events, which will commence on Monday evening, June 19, when members and their wives will participate in a wine-tasting supper party. This event will take place in the Museum of Fine Arts, and those present will have the opportunity of tasting some twelve different imported wines accompanied by a similar number of cheeses. The meal will be rounded out with special hors d'oeuvres and pastries. On Tuesday evening, the Annual Dinner to the General Council will take place in the Ballroom of the Queen Elizabeth Hotel, and special musical entertainment has been arranged for this occasion. All are invited. The highlight of our convention week will be the Annual General Meeting, which will commence at 8.15 p.m. on Wednesday, June 21. At this time the colourful ceremony of the installation of the President will take place; and His Excellency Major-General Georges P. Vanier, D.S.O., M.C., C.D., Governor General of Canada, will be made an honorary member of the C.M.A. It is interesting to note that this is only the third time in the history of the C.M.A. that a non-medical person has been awarded this honour. The other two honorary memberships were presented to the Right Honourable Vincent Massey, former Governor General of Canada; and His Royal Highness The Prince Philip, Duke of Edinburgh. In addition to the above, the Canadian Medical Association will honour its Senior Members who have been nominated by their respective Divisions.

Details of the ladies' program will appear in a later edition of the Journal along with other program highlights.

BIENVENUE À MONTRÉAL

C.M.A. delegates visiting Montreal for the first time will find it historical and gay. On every side you will encounter the bilingual character of Montreal—in

speech, in press, in street names and signs, in cuisine and entertainment.

Montreal was originally the site of the Indian village of Hochelaga, and was founded as the city of Ville Marie de Montréal, on May 18, 1642, by Paul de Chomedy, Sieur de Maisonneuve. It was incorporated as the City of Montreal in 1832, and was the seat of the Government of Canada for several years after the union of Upper and Lower Canada in 1841. Today Montreal has a population of more than 1,700,000 of which two-thirds are of French origin.

Montreal has many points of interest for the out-of-town visitor. One of the city's chief attractions is St. Joseph's Oratory, a shrine dedicated to Brother André, which is visited by some three million people each year. Other points of interest include: Château de Ramezay, Montreal's well-known museum; Lookout Point at the top of Mount Royal; the Botanical Gardens; Dominion Square; waterfront and harbour; and the Montreal Museum of Fine Arts, which has regular presentations of various types of art and culture.

On the lighter side, Montreal is reputed to have more night clubs per capita than any other city in North America; and it is famous for its cuisine. Many of the cafés, night clubs and restaurants are located in a very compact area in the heart of the city.

More about Montreal in subsequent issues.

REFRESHER COURSES AND INCOME TAX

The Committee on Income Tax has presented the following submission to the Honourable the Minister of Finance with a view to obtaining an appropriate amendment to the Income Tax Act to permit practising physicians to deduct the expenses of attending refresher courses. The presentation was supported by verbal discussion and, although no commitment was made, your Committee is hopeful that legislative action may follow. Copies of the brief have been distributed to all members of Parliament.

January 27, 1961

The Honourable Donald Fleming
Minister of Finance
Ottawa, Ontario

Dear Mr. Fleming:

Re: DEDUCTION OF EXPENSES FOR REFRESHER COURSES

1. The purpose of this submission to you by the Canadian Medical Association is to request an amendment to the Income Tax Act to allow a deduction of expenses for refresher courses incurred by medical practitioners.

2. Our Association has 14,500 members. Practically all of the profession is enrolled with us. Both urban and rural doctors from coast to coast belong to our Association.

3. The Canadian Medical Association, particularly in recent years, has been active in encouraging its members to keep up to date in their profession. Developments and new discoveries recently in our field have been so rapid and significant that refresher courses have become a practical necessity for him who pretends to keep abreast with the latest knowledge in the medical profession. We have been greatly helped and encouraged in our objective by the co-operation and initiative of leading medical schools and hospitals in offering a wide variety of excellent short courses in special fields of work (see appendix).

4. The College of General Practice of Canada, which is dedicated to the maintenance of the highest standards of medical practice in its field, has a requirement that continued membership is dependent on proof that the individual has taken one hundred hours of post-graduate refresher instruction every two years.

5. The acquisition of new knowledge and skill is a matter of considerable importance for Canadians in all walks of life, but in the case of physicians it is of vital concern not only for them as individuals but for the health of the nation. We think there is full recognition by the Federal Government of the objectives of our Association in concerning itself generally with the health of our people. The Department of Health and Welfare was established in 1944 and it is a matter of record that in the past decade Health Grants by the Federal Government have amounted to no less than $348.5 million, with $63.6 million committed for in the current year. We think that this is money well spent and the latest figures are evidence that your Government is particularly sympathetic with our objectives. We suggest that granting our request would be an eminently logical and economical method of promoting still further the program for better health in Canada.

6. Quite apart, however, from the coincidence of our aims with those of the Government, we think that our case rests on solid ground within the covers of the Income Tax Act itself. Our argument is this.

7. The Act defines "business" to include a profession (Section 139 (1) (e)). Accordingly a physician is taxed on the profits from his business, and all the rules in computing profit from an ordinary industrial or commercial business should apply likewise to him. Current expenditures of business operations are, of course, allowed as deductions and certain capital expenditures may likewise be taken into account. For the physician, capital cost allowances for professional equipment and office furniture are granted, just as for the industrial concern the cost of plant, machinery and equipment may be amortized. Most other capital costs may not be deducted but special provision has been made for certain specific kinds of expenses that are capital in nature.

8. For example, in Section 11 (1) (cb) there is specific authority for deducting an expense incurred in the year "in the course of issuing or selling shares" or "in the course of borrowing money used by the taxpayer for the purpose of earning income". This means simply that the ordinary business concern in computing annual profits may deduct the cost incurred in the year in acquiring new capital for its business.

9. The expenditures incurred by the physician in acquiring new knowledge, skills and techniques for carrying on his profession, which by law is a business,

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are exactly in the same category as the expenses of the business concern incurred in acquiring new capital.

10. As you know, in 1951 three physicians, Drs. Francis, MacLean and Gridley, took their claims for deduction of expenses incurred in refresher courses to the Income Tax Appeal Board. None of them succeeded. Generally, the main expenses were held by the Board to be capital in nature, incurred once and for all for a lasting benefit.

11. Our Association is willing to accept this conclusion of the Appeal Board that these expenses in question are incurred by the physician in the course of acquiring new capital for his business, that is, new knowledge and skills which undoubtedly are the main capital of a professional man. However, in accepting the conclusions of the Appeal Board regarding the nature of these expenditures we think we may properly assume that they will thereupon be allowed to qualify for a deduction through a specific amendment, say 11 (1) (cc), just as comparable expenses of ordinary business concerns are allowed to be deducted under Section 11 (1) (cb).

12. One further point needs to be noted. In the case of Gridley *vs.* M.N.R., Mr. Fisher stated that "the knowledge gained by him is as much a capital asset as the knowledge gained by him when he took his original medical course which enabled him to obtain a licence to practise". We agree that the new knowledge is as much a capital asset as that originally acquired, but we suggest that for tax purposes they are quite distinct and separate. The original expenses for an education were not incurred by a person carrying on a business. The student may never carry on a business. The expenses for refresher courses, however, are incurred by a business man while carrying on his business and are incurred directly for the purpose of earning profits from his business. Accordingly, an allowance for expenses of refresher courses which should be allowed establishes no case whatsoever for taking original educational expenses into account at all.

13. While merely laymen in matters of tax administration, we can see no difficulty in the way of giving effect to an allowance for expenses of refresher courses. The Tax Department has to deal constantly with expense accounts of those away from home on business. Tuition and other fees for the courses which we are discussing at universities or hospitals, and the status of the courses offered, are all matters which are easily verified. All in all, we see nothing new or extraordinary in the administration of the provision which we are requesting, and we will be happy to discuss with your officials the terms of any regulations which appear to be appropriate.

14. Our members feel that they are not being fairly treated under the law as it now stands. They readily accept the proposition that the physician is in effect carrying on a business. They feel very strongly, however, that this status should carry with it for them the same benefits of deductions which are allowed to the ordinary industrial or commercial business enterprise in acquiring new capital for the purpose of earning income.

Yours sincerely,

N. J. BLAIR, M.D.,
G. E. CHALMERS, M.D.,
For the Committee on Income tax
A. D. KELLY, M.D.,
General Secretary,
Canadian Medical Association.

APPENDIX — POSTGRADUATE COURSES

Title of course	*Location*	*Starting date*	*Ending date*	*Fee*	*Apply to*
Surgery } one day Medicine } overlap	B-Lecture Hall, Faculty of Medicine Bldg., Vancouver General Hospital	February 13 February 15	February 15 February 17	$25.00 ea. ($40.00 both)	Committee on Postgraduate Education, Medical Administration Office, Vancouver General Hospital
Pediatric, Obstetrical and Gynecological Refresher Course	University Hospital, University of Sask., Saskatoon, Sask.	February 16	February 18	$10.00	Dr. J. W. Gerrard or Dr. A. B. Brown, University Hospital, Saskatoon, Sask.
Obstetrics and Gynecology	Jubilee Auditorium, Edmonton, Alta.	March 6	March 7	$25.00	Secretary, Alberta Division, C.M.A., 501 Alexandra Bldg., Edmonton, Alberta
Eye Surgery Clinical Meeting	Dept. of Ophthalmology, University of Toronto	March 20	March 22	$50.00 (Canadian funds)	Director, Division of Postgraduate Medical Education, University of Toronto.
Annual Essex County Surgical Clinic	Cleary Auditorium, Windsor, Ontario	April 26	April 28	$25.00	Registrar: Essex County Surgical Clinic, 301 Canada Building, Windsor, Ontario
Accident and Emergency Course	Royal Victoria Hospital, Montreal	May 25	May 27	$40.00	Postgraduate Board, Royal Victoria Hospital, Montreal

PUBLIC HEALTH

SURVEILLANCE REPORTS OF EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES

POLIOMYELITIS

Canada

The preliminary total number of paralytic poliomyelitis cases reported in 1960 in Canada now stands at 820. Seventy-two fatalities were reported during the same period.

The number of aseptic meningitis cases reported in 1960 was 604.

Virological studies have been reported so far in 309 cases of paralytic poliomyelitis and 167 cases of aseptic meningitis. Among the paralytic cases, Poliovirus type III appears to have been the prevalent strain in Quebec and Saskatchewan. An increase in the type III recoveries was also reported from Alberta, Manitoba, British Columbia and Ontario.

The most frequently isolated viruses among the aseptic meningitis cases in the Province of Quebec were Poliovirus type III and Coxsackie B2, while in British Columbia, Coxsackie B5 was the epidemic strain for aseptic meningitis. (During the 1959 poliomyelitis epidemic in Quebec, Coxsackie B5 was the epidemic strain among the aseptic meningitis cases.)

PARALYTIC POLIOMYELITIS: VIRUS ISOLATIONS, 1960 (PRELIMINARY) AND 1959

Poliovirus	*Type I*	*Type II*	*Type III*	*Total*	*Negative*	*Total*
Cases.....	162	1	106	269	40	309
Per cent (1960)....	60.2	0.4	39.4	100.0	13.0	—
Per cent (1959)....	85.8	2.9	11.2	100.0	—	—

The accompanying tables present a comparison between the preliminary virological findings in 1960 and the 1959 isolations.

ASEPTIC MENINGITIS: VIRUS ISOLATIONS, 1960 (PRELIMINARY) AND 1959

Virus	*Poliovirus*	*Coxsackie*	*ECHO*	*Total*	*Negative*	*Total*
Cases.....	21	88	9	118	49	167
Per cent (1960)..	17.8	74.6	7.6	100.0	29.3	100.0
Per cent (1959)..	70.8	20.8	8.4	100.0	—	—

EPIDEMIC DIARRHEA OF THE NEWBORN

Six cases of diarrhea among newborns have been reported from a hospital in Nanaimo, B.C. The first case, in an infant who was being fed by gavage, occurred at the end of December and five other cases were reported afterwards. The agent has not been identified.

BACILLARY DYSENTERY

An outbreak of dysentery has been reported near the town of Hinton, Alta., accounting for 11 cases. The initial cases were in a Metis family living outside the town, who drank water from a contaminated well. The other patients were probably contacts of a son who attended one of the Hinton schools.

Indian and Northern Health Services

In November 1960, a mother was admitted from an Indian Reserve to Fort Qu'Appelle Indian Hospital, Saskatchewan, suffering from shigellosis. Six days later, her child was also admitted with the disease. Shortly afterwards, a child in hospital and two members of the nursing staff developed shigellosis. A considerable number of cases of diarrhea have also occurred in the Punnichy area, in which there was one proven case of shigellosis. The sudden development and the increase in Flexner-type dysentery are in the non-Indian as well as the Indian population.

GASTROENTERITIS

An outbreak of gastroenteritis has been reported from Montagnais, in Saguenay County, Quebec. Among the population of about 1200, 83 cases have been reported, of which 34 are in children in the age group 0-4, and 49 are in older children and adults. There have been two deaths, in infants, aged 2 and 3 months. The epidemic is now in full swing and more deaths may be expected. Pathogenic *E. coli* has been isolated from some stools.

INFECTIOUS HEPATITIS

The outbreak of infectious hepatitis at the R.C. Hostel for children, at Inuvik, N.W.T., has now accounted for a total of 39 cases.

ASEPTIC MENINGITIS: VIRUS ISOLATIONS, 1960 (PRELIMINARY) AND 1959

Virus	*Poliovirus*				*Coxsackie*				*ECHO*			
Type	*I*	*II*	*III*	*Total*	*B5*	*B2*	*Others*	*Total*	*6*	*20*	*Others*	*Total*
Cases.....	6	—	15	21	32	50	6	88	8	1	—	9
Per cent (1960)..	28.6	—	71.4	100.0	36.4	56.8	6.8	100.0	89.9	11.9	—	100.0
Per cent (1959)..	70.6	6.2	23.1	100.0	88.7	—	11.3	100.0	61.1	5.5	33.4	100.0

INFLUENZA

During the month of December 1960, 256 cases of influenza were reported in the Sydney, Cape Breton North, Cape Breton South and Glace Bay regions of Nova Scotia.

Epidemiology Division, Department of National Health and Welfare.
Ottawa, January 14, 1961.

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OBITUARIES

DR. ALBERIC MARIN

AN APPRECIATION

Dr. Alberic Marin was one of the few full Professors of Dermatology in Canada. He attracted an able group of juniors to his service and supervised their training. His influence has been felt throughout Canada for many years. He was highly respected by his English-speaking colleagues, and when the Montreal Dermatological Society was founded, he was not only a founding member, but took an active part in this Society from its inception. Although he was not a founder of the Canadian Dermatological Association, he was one of the earliest members to be elected to this society. He took an active part in all the affairs of the Society, and while he had been less active in recent years, his presence was always felt. It was through his example and direction that members of the Montreal Society too became members of the Canadian Dermatological Association and they in turn have played active roles in these two organizations. It may truly be said that Dr. Marin made these Societies bilingual, and in few other Societies is there such mutual understanding and good will between the English and French Canadians. Dr. Marin won honours in many fields, as others will testify, but the cordial relationship and the camaraderie which exist in these Societies between these two groups stands as a tribute to him.

R. ROY FORSEY, M.D., F.R.C.P.[C],
Historian, Canadian Dermatological Association

DR. BRUCE ANDERSON, aged 53, died suddenly in his office in Alliston, Ont., December 14. A graduate of Queen's University in 1940, Dr. Anderson practised in Alliston for 13 years and also served as coroner of Simcoe County.

Surviving are his widow and three daughters.

DR. PAUL BRASSARD, aged 47, died December 22 in Roberval, Quebec. The son of the late Dr. Hubert D. Brassard, he received his degree in medicine from Laval University in 1937. He studied in Europe and specialized in surgery on his return to Roberval.

Surviving are his widow, a son and a daughter.

DR. GEORGE DOUGLAS CHOWN, of Mirror, Alberta, died December 9 at the age of 70. After graduating from Queen's University in 1914, he practised in Erskine, Alta., and in Mirror. He served in the Medical Corps during World War I.

Surviving are a son and a daughter.

DR. GEORGE GILBERT CLEGG, aged 73, died December 2 in Kingston, Ont. A graduate of Queen's University in 1914, he was a founder of the Ontario Crippled Children's Society and its second president.

Dr. Clegg was superintendent for seven years of Victoria Hospital, London, Ont., worked for the Department of Health and Welfare in Toronto, and the Department of Veterans Affairs and conducted a private practice in Kingston. He served as a medical officer in both world wars.

Surviving are his widow, a daughter and two sons.

DR. ALBERT L. COURVILLE, aged 60, died December 20 at Montreal General Hospital. A graduate of McGill University in 1930, he had practised in Albuquerque, New Mexico, for the past 15 years as an eye, ear and nose specialist. Dr. Courville served as a medical officer in the United States Air Force during World War II.

Surviving are his widow and two daughters.

DR. A. ERNEST DOULL, aged 56, died suddenly January 7 in Halifax, N.S. Born and educated in Halifax, Dr. Doull graduated from Dalhousie Medical School in 1928 and did postgraduate study at Harvard Medical School. He returned to Halifax to practise with his father, Dr. Arthur E. Doull, as an ear, eye, nose and throat specialist.

Surviving are his widow, three daughters, one son and his father.

DR. ISAAC DUBNOV, aged 59, died in Vancouver General Hospital, December 12. Born in Russia, he came to Canada in 1912, and graduated from the University of Manitoba Medical School in 1925. He practised in Beausejour, Man., and in Vancouver.

Surviving are his widow, two daughters and one son.

DR. FREDERICK WALTER FITZGERALD, aged 54, died suddenly January 8 at his home in Lachute, Que., where he had practised for the past 23 years. A graduate of McGill University in 1933, he took postgraduate studies at Cook County Hospital and Northwestern University in Chicago.

He practised in Cornerbrook, Nfld., and in Lachute where he served as mayor.

Dr. Fitzgerald is survived by his widow and two daughters.

DR. J.-EMILE FORTIN, aged 75, died January 9 in Quebec. A graduate of Laval University in 1909, Dr. Fortin practised in the Thetford Mines area for 50 years.

Surviving are five sons, including Dr. Claude Fortin, and two daughters.

DR. ALDERIC LAURENDEAU died in Hôtel-Dieu Hospital, Montreal, January 11, at the age of 70. After graduating from the University of Montreal, he returned to his birthplace, St. Gabriel de Brandon, to carry on the practice established by his grandfather, the late Dr. Olivier Laurendeau, in 1850 and his father, the late Dr. Albert Laurendeau. On calls to outlying areas he used an aeroplane in contrast to his grandfather's practice of travelling by horseback. Dr. Laurendeau served as mayor of St. Gabriel de Brandon for a number of years and also as Liberal Member of Parliament.

Surviving are his widow and two daughters.

DR. LORNE J. STUART, aged 72, died December 13 in Scotland, Ont. After graduating from McGill University in 1917, he served with the Canadian Army and practised in Morriston and Scotland, Ont.

Dr. Stuart is survived by his widow.

BOOK REVIEWS

IMPORTANCE OF THE VITREOUS BODY IN RETINA SURGERY WITH SPECIAL EMPHASIS ON RE-OPERATIONS. Edited by Charles L. Schepens. 226 pp. Illust. The C. V. Mosby Company, St. Louis, Mo., 1960. $15.00.

This book might well be considered as the Transactions of the Second Conference of the Retina Foundation, Boston, which was held in Ipswich, Mass., in May 1958. The roster of speakers sounds like a rundown of who's who in the field of retinal detachment both in America and Europe. What has resulted is a beautifully produced and illustrated authoritative volume covering the latest advances, and even thoughts, in this most difficult and tantalizing field.

Nothing has altered Gonin's original precept that the development of a retinal hole is the crucial event leading to detachment, and in bringing about a cure, our first aim must be to close the hole. Leber, Gonin, and later Lindner, in particular, drew attention to the importance of the vitreous and the pathological changes in it, in the development and treatment of this disturbance. In the selection of the proper surgical procedure in the first instance, and in understanding the reasons for failure and how one may attempt to succeed on a second occasion, full understanding of the role of the vitreous is essential. The present volume may be considered to represent the very latest authority in this matter. A complete description and discussion of the latest findings dealing with the structure of the retino-vitreal attachments, the cortical region of the vitreous, and the formation of the vitreal membranes are presented. Many of these discoveries are of the most recent order and are of vital importance. Various surgical approaches for the correction of retinal detachment, and in particular the handling of redetachments, are fully described and discussed by recognized experts. All has been edited by Dr. Charles L. Schepens in a masterly way. This volume is recommended for all ophthalmologists.

CLINICAL OBSTETRICS AND GYNECOLOGY, Vol. 3, No. 3. Special Articles: Frigidity—Dr. Edward C. Mann; The Obstetric Forceps, Puerperal Fever, Gynecology Becomes a Surgical Specialty—Harold Speert. Bleeding and Hemorrhage in Late Pregnancy. Edited by R. Gordon Douglas. 188 pp. Illust. Paul B. Hoeber, Inc., New York, 1960. $18.00 (subscription of four books for a period of one year).

This is the third book for 1960 of the quarterly publication of "Clinical Obstetrics and Gynecology"; the eleventh in this highly valuable series devoted to the clinical side of this specialty. As in the earlier volumes, this publication contains a symposium and a series of special articles. Each symposium has a well-known guest editor, and each subject is divided into as many aspects as will cover the problem thoroughly.

Most of this book deals with "Bleeding and Hemorrhage in Late Pregnancy", under the editorship of R. Gordon Douglas, Professor of Obstetrics and Gynecology, Cornell University Medical College, New York, who has contributed an excellent chapter on "Prophylaxis, Initial Management and Diagnostic Procedures". Ten other contributors cover, adequately but briefly, every possible aspect of this important problem from placenta previa and premature separation of the placenta to coagulation defects and delayed complications of hemorrhage.

It is interesting to note that Dr. Stromme found that out of 16,488 deliveries at the New York Lying-In Hospital, one out of 41 patients had some bleeding in the last trimester due to "other than major obstetrical causes". Dr. Ware emphasizes the serious responsibility of the obstetrician when deciding to perform a patient's first Cesarean operation and the subsequent danger of rupture of the scar. Dr. Cole stresses the need of an obstetrical blood bank containing two bottles of O-negative blood treated with Witebsky's soluble blood-group specific for A and B substance. Dr. Russell warns of the dangers of hepatitis following fibrinogen injection and provides an excellent "flow sheet" which should be in every obstetrical department. He states: "The single most important point in the diagnosis is a high index of suspicion."

The special article on "Frigidity" is well worth careful reading, as this is a subject that is inadequately understood by the profession at large and yet is the cause of much distress and unhappiness. Dr. Speert's three short historical notes on "The Obstetric Forceps", "Puerperal Fever" and "Gynecology Becomes a Surgical Specialty" will give pleasure to most physicians.

This book, in fact the whole series, should be in every medical library, and most physicians (general practitioners and specialists alike) will find them most valuable.

PSYCHOANALYTIC CONCEPTS OF DEPRESSION. Myer Mendelson. 158 pp. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $7.25.

This is a valuable little book for those who are interested in psychodynamics and in the dynamics of depression in particular. A comprehensive review has been made of the theories originated by most of the past and present captains of this branch of psychiatry. In chapter 4, the author attempts to elucidate the similarities and also the differences of these theories. While the similarities are many, the differences are so great that, as the author points out, one wonders whether the same entities are being discussed by the theorists. Logically the author then moves on to the question of diagnosis. He states, "Diagnostic entities are not now accorded quite the same respectful attention in psychiatry as they are in other medical specialties." Hopefully, your reviewer read on, but his hopes of reading about the signs and symptoms on which the diagnosis and differential diagnosis of "depression" can be made were not fulfilled. The author was sadly unable to resist the attraction of causative theories.

In the concluding chapter the author outlines some of his conclusions and hopes for the future. The review can best be concluded in his words: "It would have been pleasing to be able to report that this body of literature represented, in essence, a progress through the years of a Great Investigation. It does so in part, but perhaps even more it represents a Great Debate with the rhetorical rather than scientific implications of this word. Indeed at times it bears the stigma not of an exchange of ideas but of a monologue—a not-so-great monologue."

Canad. M. A. J.
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ACTIVE ALERTED POSTURE. W. E. Tucker. 61 pp. Illust. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Limited, Toronto, 1960. $1.80.

This little monograph deals with the effects of bad posture.

The first half is devoted to the basic principles of posture, skeletal types, and elementary muscle physiology. There is a chapter on the mechanics of posture which is very well illustrated by line drawings of simple comparisons depicting all joint groups affected by posture. The conclusions reached here are worth thinking about. The bad results of poor posture are thoroughly discussed.

Once the preliminary facts have been presented, the author delivers his message.

The text is simple, well organized and easy to read; the print is neat and the headings are in bold type; the illustrations are clear and the references quite adequate.

This is a stimulating little book and all associated with medicine would be rewarded by reading it.

AIDS TO BIOCHEMISTRY. S. P. Datta, Reader in Biochemistry in the University of London, and J. H. Ottaway, Senior Lecturer in Biochemistry, University of Edinburgh. 266 pp. Illust. 5th ed. Baillière, Tindall & Cox, London; The Macmillan Company of Canada Limited, Toronto, 1960. $2.50.

The fifth edition of this well-known series is published twelve years after the previous edition. Up-to-date and clearly written, it shows the remarkable growth of biochemical knowledge in recent years. It should be useful to medical students and to postgraduate students preparing for certification and fellowship examinations. This book is an excellent summary, but it clearly cannot take the place of laboratory and practical notes for the medical student, a function for which it was not designed. The reviewer found the chapters on Detoxication and Excretion, Biochemical Variants, and The Common Terminal Pathway of Metabolism, to be particularly interesting.

BIOLOGY OF THE PLEUROPNEUMONIA-LIKE ORGANISMS. Annals of the New York Academy of Sciences, Vol. 79, Art. 10. D. G. F. Edward (Conference Chairman). Pp. 305-758. Illust. Published by the Academy, 1960. $5.00.

This book is a review of the pleuropneumonia-like organisms and has been written by many collaborators under the chairmanship of D. G. F. Edward. It is composed of six parts. The first part deals with the morphology and classification of these organisms. Particular attention is given to the L-phase of bacteria in relation to the PPLO. The other parts deal with the isolation, propagation, physiology, serology and chemotherapy of these fastidious micro-organisms. The last part examines the human pathology caused by these agents.

The book is illustrated with photographs, diagrams, charts and graphs. Each section contains many references.

This book is a comprehensive review of a difficult field of bacteriology, and the increasing interest regarding the PPLO as possible responsible agents in many pathological conditions will be well appreciated by biologists, students and research workers.

THE CLINICAL USE OF ALDOSTERONE ANTAGONISTS. Compiled and edited by Frederic C. Bartter. 208 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $5.50.

This symposium is a report of the proceedings of a conference on the Clinical Use of the Aldosterone Antagonists, held in Chicago, Illinois, on October 16, 1958, under the sponsorship of G. D. Searle & Co. and under the chairmanship of Irwin C. Winter, M.D., Ph.D.

Twenty-three contributors took part in the conference, each one an internationally known and respected investigator. The report has been ably compiled and edited by Frederic C. Bartter, and each paper has been well presented and technically illustrated. The discussion of each paper is pointed and constructive, and references are given at the end of each paper, and where indicated, in the discussions.

The fundamental mechanism of action and the clinical use of the aldosterone antagonists as a diagnostic tool in the study of aldosteronism are covered very completely in the first section. Other sections are devoted to the advantages and limitations of, and contraindications to the use of these agents in the presence of cirrhosis of the liver; early experience with aldosterone antagonists for patients with cardiac failure and edema; and preliminary studies with the use of aldosterone antagonists in hypertension, nephrosis and idiopathic edema.

This book should realize the hopes of the editor that it "will stimulate interest in, and promote understanding of, these agents in other areas of clinical investigative medicine." It can be recommended to clinical investigators in the fields of cardiology, renal physiology, endocrinology and diseases of the liver, as well as to practising internists who are confronted daily with the problem of edema.

ACTUALITES NEUROPHYSIOLOGIQUES. Première Série. (Current Neurophysiological Information, First Series.) Published under the direction of A. M. Monnier. 273 pp. Illust. Masson & Cie, Paris, France, 1959. $8.20 approx.

Sous ce titre le professeur A. M. Monnier a rassemblé les conférences de neurophysiologie de la Faculté des Sciences de Paris. Il va sans dire qu'il ne s'agit pas d'un cours complet de neurophysiologie mais tout simplement du traitement par des experts de chapitres de neurophysiologie qui les intéressent particulièrement, sur lesquels ils ont longuement travaillé et peuvent parler avec autorité.

Le choix des conférenciers a été fort heureux. Qu'il suffise de mentionner lord Adrian, Bonvallet, Granit, Hartline, Laporte, etc.

Les conférences ont été groupées sous quatre chefs: physiologie sensorielle; physiologie de la fibre nerveuse et des systèmes réflexes; neurophysiologie centrale et humorale; physiologie neuromusculaire et cardiaque et chacun des sujets est traité avec concision et beaucoup de clarté, sans revue harassante de littérature ni spéculation étendue. Les auteurs terminent leur travail par l'exposé des recherches en cours sur le sujet en discussion. Les illustrations et figures sont abondantes, claires et bien faites.

Les étudiants en neurophysiologie auront sans doute plaisir et intérêt à lire ces conférences qui leur sont destinées. Nous souhaitons que cette première série soit suivie de bien d'autres.

(Continued on page 460)

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KLINISCHE CHIRURGIE FUER DIE PRAXIS. In Vier Bänden. Band I, Lieferung 3. Edited by O. Diebold, H. Junghanns and L. Zukschwerdt. 618 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1960. $12.85.

The third part of Vol. I of this series of texts on the clinical practice of surgery is divided into two main sections. The first consists of a monograph on the diseases of blood vessels and lymphatics. A general introductory chapter outlines the clinical and special methods of examination, while the major part of this section is devoted to descriptions of common lymphatic and vascular diseases. The growing interest and expanding knowledge in this field are well reflected in the sound and reliable presentation. The second section of this volume contains monographs on the hypophysis, hypothalamus, thyroid, parathyroid, thymus, glomus tumours, pancreas, adrenal glands and testes. This is obviously a vast field and to condense it into a small volume is indeed an achievement. The contributors have succeeded admirably without omitting the important or belabouring the obsolete.

The excellent illustrations and x-ray reproductions and a most up-to-date collection of references make this an especially useful book for the surgeon with a knowledge of German.

KLINISCHE CHIRURGIE FUER DIE PRAXIS. Band III, Lieferung 2. Edited by O. Diebold, H. Junghanns and L. Zukschwerdt. 360 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1960. $9.50.

This section of the Clinical Practice of Surgery series concerns the stomach and duodenum. After a general introduction devoted to anatomy, physiology and clinical procedures there are separate monographs on gastritis, peptic ulcer, tumours and congenital and traumatic lesions. Operative treatment is mentioned briefly but with useful discussions of the problems of early and late postoperative complications.

As one would expect, the discussion of peptic ulcer receives the greatest prominence. The author describes in detail his own theory of the pathogenesis of peptic ulceration in addition to those previously recorded. He observes that common to all recorded observations, experimental results and theories of ulcer pathogenesis are the simultaneous and interrelated factors of disturbed gastric motility and secretion. These changes cause an increase of night secretion and result in gastritis. Hypersecretion leads to increased irritability of the pyloric mucosa, establishing the vicious circle of hypersecretion → delayed emptying → gastritis. The erosion thus produced may progress to ulceration.

The importance of stress in ulcerogenesis is mentioned, and though the stress → hypothalamus → endocrine mechanism is discussed (Curling's ulcer), the role of the vagus is not.

All in all, the subject is well covered in the space provided. The statements reported in this book are sound, but it is too abbreviated for those with specialized interests in this subject. The references are taken mostly from the German literature and do not give a fair picture of the extensive Anglo-American contributions in this field.

EARLY IDENTIFICATION OF EMOTIONALLY HANDICAPPED CHILDREN IN SCHOOL. Eli M. Bower. Edited by Molly Harrower. 115 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $6.00.

The author describes a study designed to screen emotionally handicapped children in the school classroom. Approximately 5500 children attending school in the State of California were rated. Two hundred teachers participated in the project. A group of 200 children who had been seen and diagnosed previously as "emotionally handicapped" by the school psychiatric and psychological services were selected. They were enrolled in the classes of the participating teachers. The teachers were not told which children had been diagnosed as "emotionally handicapped".

The screening procedure consisted of self, group and teacher ratings. The handicapped children were subsequently compared with their classmates with respect to age, absenteeism, socioeconomic status of father, intelligence and achievement in reading and arithmetic.

The rating procedures are well outlined. The appendix to this volume includes the rating forms and the instructions for their administration. In at least one of the rating forms an attempt is made to correlate items to determine which ones are useful in distinguishing emotional handicaps, an important feature of any test.

The emotionally handicapped children scored significantly lower on group Intelligence Quotient tests but on individual tests approached the mean. They scored lower on reading and arithmetic achievement tests. Emotionally handicapped boys showed more self-dissatisfaction than girls. Other children saw the emotionally handicapped child as hostile, inadequate and negative. Socioeconomic factors did not appear to be significant. The classroom teachers were able to rate 87% of the emotionally handicapped children correctly.

A random group of 225 children screened by the study were then selected for examination by clinical psychologists. Ninety per cent of this group were found to have moderate to severe emotional problems on individual clinical assessment.

Another study was designed to determine whether or not a clinician could effectively distinguish a normal from a handicapped child on the basis of an individual examination. Two clinical psychologists examined a group composed of screened and unscreened children. Specific results are not given but the author reports that the data significantly distinguished the two groups, i.e. the clinician can recognize a normal child when he examines one.

The book is well written. The samples used as a basis of the study are large. Many statistical results are given. The book was written primarily for school administrators, trustees and teachers, to demonstrate the part the school can play in mental health problems of children. The book is well referenced and includes a good review of the literature.

There is a need to develop screening procedures that will detect emotional handicaps early. The procedure should be brief, reliable and reproducible. The items should be validated as to their appropriateness. This project would appear to be a step in the right direction. One hopes that there will be forthcoming publications directed to mental health workers and researchers, giving the plan and results of this study in more detail.

MEDICAL NEWS *in Brief*

(Continued from page 442)

POSTGRADUATE COURSE ON INTERNAL MEDICINE (SELECTED TOPICS), AMERICAN COLLEGE OF PHYSICIANS

Postgraduate Course No. 8 of the American College of Physicians, "Internal Medicine: Selected Topics", will be given at McGill University School of Medicine, Montreal, from March 13 to 17, 1961, under the direction of W. H. Philip Hill, M.D., F.A.C.P.

The first day of the course will deal with pulmonary and cardiovascular problems, the second with renal disease, the third with endocrine and metabolic disorders, the fourth with hematology and the fifth with a miscellaneous group of conditions and will include a clinico-pathological conference. The main emphasis will be placed on recent developments in clinical medicine, clinical physiology and certain newer diagnostic techniques. Panel discussions and symposia will be used freely. The guest faculty consists of John B. Dossetor, B.M.(Oxon), M.R.C.P.(Lond.), F.R.C.P.[C], Post-Doctoral Research Fellow, New York Medical School; Jacques Genest, M.D., F.A.C.P., F.R.C.P.[C], Associate Professor of Medicine, University of Montreal, and Director of Clinical Research, Hôtel-Dieu; and Guy Lemieux, M.D., Markle Scholar in the Medical Sciences, and Assistant Professor of Medicine, University of Montreal. The officers of instruction will consist of 60 members of the Medical Faculty of McGill University.

The fee for the course is $60.00 for A.C.P. members, and $80.00 for non-members. Registration forms and further information are available from: The American College of Physicians, 4200 Pine St., Philadelphia 4, Pa.

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TWENTY-FIFTH ANNIVERSARY PROGRAM: THE CANADIAN PHYSIOLOGICAL SOCIETY

The Canadian Physiological Society is planning a special program in celebration of its 25th anniversary in 1961. To mark the anniversary the Society has elected its first six honorary members. These are Sir Henry Dale (London, England), Dr. Laurence Irving (Anchorage, Alaska, U.S.A.), Professor E. J. King (London, England), Professor Henri Laugier (Paris, France), Dr. E. W. R. Steacie (Ottawa, Canada) and Professor A. E. Wilhelmi (Atlanta, Georgia, U.S.A.).

It is planned to have as many as possible of the newly elected honorary members attend the Fourth Annual Meeting of the Canadian Federation of Biological Societies in Guelph in May and June of 1961 to participate in these activities. The Board of the Canadian Federation of Biological Societies has graciously permitted the Federation Symposium and the Federation Dinner of the 1961 Annual Meeting to be organized by the Canadian Physiological Society to mark its 25th Anniversary.

The 25th Anniversary Committee of the Canadian Physiological So-

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MEDICAL NEWS *in brief*

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ciety, appointed last year, plan that the Federation Symposium be given by three of the newly elected honorary members and that a fourth honorary member be the main speaker at the Federation dinner. These plans have been approved by the Council and will be confirmed upon consent of the honorary members concerned. Each honorary member will be asked to speak briefly when he is presented with his diploma and other symbols of honorary membership.

—

FORTY YEARS OF INSULIN

The September 1960 issue of *The British Medical Bulletin* (publishers: Medical Department, The British Council, 65 Davies Street, London, W.1) is devoted to a symposium on insulin. The *Bulletin's* scientific editor, F. G. Young, gives a brief review of the history of diabetes and of the preliminary discoveries that eventually led to the isolation of insulin by Banting and Best. It also refers to the more important phases of research in diabetes over the past forty years. As is fitting, the article on the history of insulin was written by Professor C. H. Best. There is also a paper by F. Sanger, which is a slightly expanded version of the lecture he delivered on the occasion of his receiving of the Nobel prize for elucidating the complete chemical structure of insulin. Other papers in this issue were contributed by Vallance-Owen on the subject of insulin antagonists and by Wright on insulin antibodies. The action of insulin on carbohydrate metabolism, fatty acid metabolism, insulin and protein metabolism and the mechanism of action of insulin are other topics discussed by authorities in these respective fields. It is of interest that the final papers deal with synthetic hypoglycemic substances and the clinical effectiveness of insulin substitutes.

—

FINANCIAL ASSISTANCE AVAILABLE FOR GRADUATE STUDY IN MEDICINE

A booklet entitled Financial Assistance Available for Graduate Study in Medicine, just published by the Association of American Medical Colleges, can be purchased for $2.50 from AAMC headquarters, 2530 Ridge Ave., Evanston, Ill. The 1960 revised edition is designed to aid both foreign and North American students seeking graduate and fellowship opportunities primarily in the United States and Canada. It is a comprehensive manual containing information on fellowships, funds, and prizes offered by foundations, professional organizations, federal agencies, and U.S. and Canadian medical schools.

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COMMUNICATION FROM THE AMERICAN COLLEGE OF RADIOLOGY

Several months ago, the American College of Radiology received inquiries from many editors of state and other medical society journals relative to the American Society of Diagnostic Radiology

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MEDICAL NEWS *in brief*

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which was then being promoted by Dr. Louis Shattuck Baer, a California internist. Correspondence with Dr. Baer revealed that that society had no constitution, bylaws or officers. The aims of the society were variously described in different communications.

More recently, the College has received inquiries relative to the American Society of Clinical Radiology, also being promoted by Dr. Louis Shattuck Baer. The College takes this means of notification that this organization has no known connection with any radiological society or group. Further, it is the opinion of the College:

1. That sufficient opportunities exist in the meetings of county, state, regional and national medical societies for the presentation of worthwhile papers and exhibits in the field of radiology.
2. That sufficient special and general medical journals now exist for the publication of meritorious medical and scientific communications in the field of radiology.
3. That the use of the term radiology in the title of an organization may unfortunately cause those not informed to identify this group as being composed of physicians who have been examined and certified to be competent in radiology by a recognized medical specialty board.
4. That medical journals and their sponsoring medical societies would be well advised to obtain full details concerning the American Society of Clinical Radiology before soliciting reader-members on behalf of Dr. Baer.

—

APPOINTMENT OF THE NEW SECRETARY GENERAL OF THE PAN AMERICAN SANITARY BUREAU

Dr. Victor Arnold Sutter, Minister of Health and Welfare of El Salvador from 1956 to 1958, has been appointed Secretary-General of the Pan American Sanitary Bureau.

The new PASB Secretary-General has a long background in international health. From 1950 to 1956 he served at the Geneva headquarters of the World Health Organization, first as Director of the Divisions of Communicable Disease and Public Health Services, and later as Assistant Director-General in charge of Advisory Services. From 1947 to 1950 Dr. Sutter served as a public health officer of the Institute of Inter-American Affairs, in the Special Public Health Service in Brazil. During 1945-46 he was Chief Medical Officer of the United Nations Relief and Rehabilitation Administration in China.

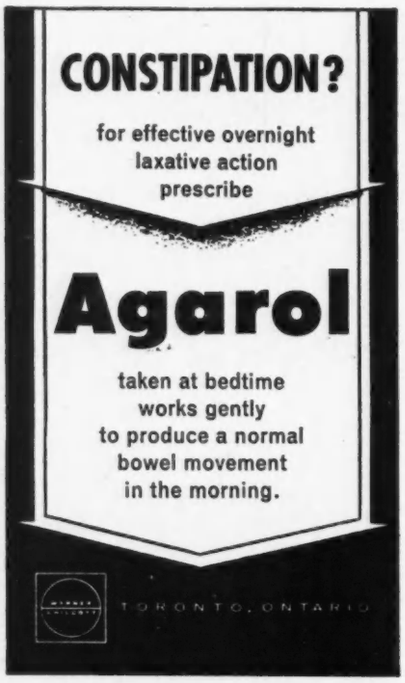
He was appointed PASB Secretary-General by Bureau Director Dr. Abraham Horwitz with unanimous approval of the Executive Committee of the Pan American Health Organization. The seven-nation committee is composed of the representatives of Argentina, Brazil, Chile, Colombia, El Salvador, Honduras, and the United States. The Committee meets on behalf of the entire PAHO membership – the 21 American Republics.

A native of San Salvador, his country's capital city, Dr. Sutter entered El Salvador's National Health Service in 1937 as Inspector General of Health, a post he held until 1939. From 1939 to 1944 he was El Salvador's Director General of Health.

Dr. Sutter received his M.D. degree from El Salvador's National University in 1927. He was awarded a Master of Public Health degree from the Johns Hopkins University in 1937.

He is a member of the Medical College of El Salvador, the Brazilian Society of Hygiene, the American Society of Tropical Medicine, and the Royal Society of Tropical Medicine and Hygiene, and Honorary Fellow of the American Public Health Association. He has been also a member of the WHO Advisory Panel of Experts on Public Health Administration.

The Pan American Sanitary Bureau is the operating arm of the Pan American Health Organization. The Bureau was founded in 1902 and is the world's oldest international health organization. Since 1949 it has also served as the World Health Organization's Regional Office for the Americas.



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AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY—CLINICAL AND ORAL EXAMINATIONS

The next scheduled examinations (Part II), oral and clinical, for all candidates will be conducted at the Edgewater Beach Hotel, Chicago, Illinois, by the entire Board, April 8 to 15, 1961. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates.

Candidates who participated in the Part I Examinations will be notified of their eligibility for the Part II Examinations as soon as possible.

The deadline date for the receipt of new and reopened applications for the 1962 examinations is August 1, 1961. Candidates are urged to submit their applications as soon as possible before that time, to the Secretary, Robert L. Faulkner, M.D., 2105 Adelbert Road, Cleveland 6, Ohio.

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POSTGRADUATE REFRESHER COURSE: INDUSTRIAL HEALTH

A postgraduate refresher course on industrial health will be held in the School of Hygiene, University of Toronto, March 6 to 9, 1961. The theme of the course will be "Early Diagnosis of Disease". The registration fee is $50.

Applications should be directed to The Director of Postgraduate Medical Education, University of Toronto, Toronto 5.